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It was reported that the plasma pharmaceuticals industry exceeded 20$ billion in market value in 2016, with U.S. donors accounting for roughly 70% of the world's collected plasma. Since being subjected to market forces blood collection and exchange have raised ethical questions about the encroachment of economic logic into previously excluded spheres. There has long been speculation that for-profit plasmapheresis centers are disproportionately located in marginalized areas, raising a need for inquiries into the ethics of spatial and commodifying processes. Despite concerns, empirical analysis on plasmapheresis clinic location has been anecdotal, dated, or emphasizing a public health perspective while mainly ignoring questions of exploitation. This paper explores the spatio-temporal development of the plasma industry across scales and perspectives, and compares empirical results to socially constructed representations of the industry.

KEYWORDS: Plasma, exploitation, public health, social geography, geography and ethics

A GEOGRAPHICAL ANALYSIS OF US PLASMA CENTERS AND THEIR ECONOMIC, SOCIAL, AND PUBLIC HEALTH IMPACTS

by

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CHAPTER I

SPATIAL ANALYSIS OF FOR-PROFIT PLASMAPHERESIS CLINICS

Abstract

It was reported that the plasma pharmaceuticals industry exceeded 20$ billion in market value in 2016, with U.S. donors accounting for roughly 70% of the world's collected plasma. During the Great Recession more than one hundred new plasmapheresis clinics opened in the United States and its total number of donations nearly doubled between 2006 and 2011. Since being subjected to market forces blood collection and exchange have raised ethical questions about the encroachment of economic logic into previously excluded spheres. A critical and geographic perspective can apprise the implications of market logic and processes on materials newly commodified by rapidly evolving technology. There has long been speculation that for-profit plasmapheresis centers are disproportionately located in marginalized areas, raising a need for inquiries into the ethics of spatial and commodifying processes. Despite concerns, empirical analysis on plasmapheresis clinic location has been anecdotal, dated, or emphasizing a public health perspective while mainly ignoring questions of exploitation. This research examines the social and economic geography surrounding for-profit plasmapheresis centers in the US in an attempt to better understand locating processes and practices.

Key words: plasma, plasmapheresis, blood, medical technology industry, predatory landscape

Introduction

The transfusion of blood components is an essential part of modern medicine. Most countries and organizations obtain blood or separated components for transfusion from donors on a voluntarily and anonymous basis. Blood supplies derived from 100% voluntary non-remunerated blood donation (VNRD) by 2025 is the goal established by the World Health Organization (Garraud and Tissot 2018). Similarly, in the US nearly all blood components intended for transfusion are collected on a VNRD basis (Farrell 2012). However, blood components intended for further manufacturing, like plasma, are mainly collected from compensated donors. Manufacturing usually yields expensive pharmaceutical products consumed by the world's wealthiest countries. Collection of whole blood is handled by public agencies or non-profit NGOs such as the Red-Cross, while plasma collection, especially in the US, is largely carried out by the private for-profit sector. The components of whole human blood are plasma (55% by volume), red blood cells (45% by volume), and white blood cells and platelets (<1% by volume). Plasma appears as a clear, yellowish liquid after all other components are removed. It is 90% water with the remainder constituted by salts, enzymes, antibodies and proteins, and contributes to clotting, material transport, and immunity. Despite current and potential commercial utility of plasma no successful synthetic alternative has been developed. Thus, before raw plasma can be manufactured into pharmaceutical goods it must first be collected from human donors.

Raw plasma is categorized as either recovered or sourced based upon method of collection. According to FDA compliance policy guidelines, recovered plasma is derived from single units of whole blood or as a by-product resulting from the preparation of blood components from whole blood collection. It is considered a material unlicensed by the FDA and is intended to be manufactured, most commonly, into pharmaceuticals and therapeutic medical

products. The for-profit blood industry collects plasma primarily, but not exclusively, from paid donors (Weinstein 2018) however, plasma collected for transfusion is unlikely to come from paid donors for two reasons. First, in the 1970s the FDA began requiring units of whole blood and components to be labeled paid or volunteer. As a result, this indirectly stopped hospitals and transfusion services use of paid blood materials (Farrell 2012; Weinstein 2018). This was primarily related to medical professionals' concern that plasma from paid donors was more likely to be infected. Second there are additional regulatory barriers concerning storage for transfusable plasma. Plasma for transfusion can take many forms but it is typically recovered and must be converted into the following products: Fresh Frozen Plasma (FFP), Plasma frozen within 24 hours after phlebotomy (PF24), and Liquid Plasma. All of these products require specific and stringent storage protocols (Roback et al. 2010; Weinstein 2018).

The second category, sourced plasma, is a licensed FDA product and is collected through a self-contained and automated process called plasmapheresis. During apheresis the plasma component is separated and collected, and remaining constituents are returned. Sourced plasma is not used in direct transfusion, and in the US supplies are maintained almost exclusively by for-profit firms collecting from compensated donors (Farrugia, Penrod, and Bult 2010; Farrell 2012). The pattern of US source plasma and recovered plasma originating almost exclusively from paid and volunteer donors, respectively, has been the case for some time (Krever 1997).

Currently hundreds of for-profit plasma clinics exist in the US. Plasma harvested from compensated donors make up a majority the raw plasma circulating in a growing international market that is currently worth over 20 billion dollars. The purpose of this research is to explore the neighborhood characteristics surrounding sites where the process of selling plasma occurs. This paper will focus on the US, first, because of its importance in the global plasma economy. Additionally, there is little research exploring the geography of bodily commodification within

formal economies of developed countries. Most existing work has focused on illicit activities or national scale case studies of less developed countries (Cohen 2001; Davies 2006; Shimazono 2007; Carney 2011; Bronwyn 2012; Healy and Krawiec 2017)

The remainder of this article is structured as follows. The next section provides an overview of the global industry, highlighting the US's role as a major exporter. The paper then discusses the policy and ethical considerations entangled with donor compensation and plasma commodification. This work has implications for policy discourse, but focuses primarily on ethical concerns, specifically how geographic analysis of spatial organization can illuminate particular economic rationales and understandings of justice. After reviewing the scant literature on plasma clinic geography, the work draws upon cognate studies of siting practices by fringe financial firms and critical GIS literature to situate and justify the analysis. Finally, details of the empirical analysis of clinic locations delineated and the implications of its results are discussed.

United States in the Global Blood-Plasma Economy

The global market owes its current lucrativeness to two historical scientific breakthroughs: fractionation and plasmapheresis. As a response to the need of blood toward war efforts in the 1940s, the US government enlisted the help of Dr. Edwin Cohn, a Harvard University protein chemist. At the time, transfusion of whole blood or liquid plasma were the only two options for treating wounded. Cohn developed the process of fractionation, a technique that allowed separation of plasma into protein-based component parts, or fractions. A result of this process was the development an important fraction called albumin, which proved to be a logistical improvement over both liquid plasma and whole blood in the treatment of wounded soldiers. The technique that came to be known as Cohn fractionation, was integral to blood component therapy in the latter half of the twentieth century (Starr 1998; Farrell 2012).

Plasmapheresis was another advancement that aided the growth of plasma collection and manufacturing from a primarily local endeavor into a global activity (Burnouf 2007). Since plasmapheresis allows for plasma extraction from donor whole blood and the retention of red and white blood cells, donors may donate plasma more frequently. According to Farrell (2012, 38), plasmapheresis "enabled the burgeoning industry to collect plasma from individuals on a weekly basis which could result in up to fifty litres of plasma being taken from a single donor on an annual basis."

Pharmaceutical products derived from plasma continued to develop as new fractions and applications were discovered. During the 1970s, the international trade in plasma grew dramatically, complete with "plasma brokers" intent on moving plasma through "spot markets" in major North American and European cities to achieve high prices fueled by international bidding (Farrell 2012, 39). The plasma protein market has steadily grown in terms of value and throughput since the late 1990s. The industry's global value grew from $4.8 billion in 1996 to $11.8 billion in 2008, reaching over $21 billion in 2016 (Wellington 2014; Hotchko and Robert 2018). The volume of plasma fractionated annually by the pharmaceutical industry has grown from 28 million liters in 1999 to 45 million liters presently, with the majority provided by paid US donors (Volkow and Del Rio 2005; Burnouf 2007; Weinstein 2018).

The world supply of plasma derivatives is dependent on US source plasma, which uses compensated donors and is exempt from the FDA's labelling requirement. In 2010, it was estimated that 51% of the world's supply of plasma for fractionation was generated by the US source plasma sector (Farrugia, Penrod, and Bult 2010). Wellington (2014) reported that US donors constituted 70% of worldwide collections. More recently, Hotchko and Robert (2018) estimated that 66% and 74% of total and sourced, respectively, came from the US. Strengers and Klein (2016) also noted the global importance of US plasma, framing it as a strategic resource

comparable to energy and potable water. The US is unique in that it has adopted an almost entirely laissez faire framework for plasma procurement. Other countries have taken decided stances on the market-based approaches to blood by either prohibiting monetary compensation or strictly limiting the number of donations allowed.

The industry's economic projections are favorable by all accounts, but its potential growth could be hampered by continued tension between for-profit plasma industry supporters and its critics. For example, there has been successful resistance efforts, framed with ethical concerns, against corporate expansion into Canada (Kingston 2017). This research examines portions of such contending claims through empirical analysis. Drawing upon Graves' (Graves 2003) concept of landscapes of predation, the site-location strategies are analyzed for for-profit plasmapheresis clinics in the US and discuss the implications these findings have for ongoing public policy and ethical discourses.

Clinic Location

Richard Titmuss's (1971) foundational work *The Gift Relationship* (TGR) was the first to bring scrutiny to the practice of paying for blood by raising questions about the links between compensated blood, public safety, and ethics. It was also the first to question public health and ethical implications of blood collection in relation to clinic locations and donor demographics.

TGR was a sociolo gical study of national blood systems originating from Titmuss's concern for distinguishing between 'social' and 'economic' types of value, and the relations each type had in influencing policy and institutions dedicated to public welfare. Titmuss describes the properties and uses of blood in modern society, and provides statistical data on supply, demand, and distribution of blood under the British and United States national blood systems in the 1960s. His work was ambitiously interdisciplinary, and its significance and breath are evident in the range of fields it impacted. It stimulated work within ethics, political philosophy, sociology,

psychology, public health, and economics. Additionally, it has been suggested that it led to major changes in US public policy during the Nixon administration (Rapport and Maggs 2002).

The results of his analysis suggested the human motivations underpinning the giving of blood and plasma were complicated, and for interpretative guidance he drew upon anthropological and sociological theories of gift giving in 'primitive' societies. His research led him to advocate for national blood policy predicated on a gift relationship in lieu of one based upon market principles, dependent upon compensated donors (Rapport and Maggs 2002; Farrugia, Penrod, and Bult 2010). Titmuss made two major claims that resonated among academics and policy makers. First, blood and plasma collected from VNRD was more economically efficient and consistently safer from contamination. Second, he argued that paid donation was ethically objectionable because it contributed to unfairness and exploitation, that it eroded social solidarity, and crowded out potential donors motivated by altruism (see Sandel 2012 for a philosophical treatment of Titmuss's arguments, especially as it pertains to solidarity and crowding out donors).

Despite its lasting influence there are concerns over Titmuss' methodologies, conclusions, and present relevance. Mclean (2010) notes the major errors in his methodology but maintains Titmuss's work is as relevant as the day it was written. Mclean also suggests that TGR protected the principle of non-market blood supply in the UK and induced US administrations to discourage a national blood system that is entirely market dependent (i.e., prevented selling of whole blood). Representatives of the for-profit arm of the industry, along with advocates of using market mechanisms to incentivize plasma donation remain critical of TGR (for examples of a libertarian defense of market mechanism see Taylor 2005, 2012, 2014b, 2015). Farrugia et al (2010) maintain that the influence of TGR is much exaggerated, arguing that steps to phase out

paid donation in the developed world were independent of TGR, though this opinion would be in the minority.

Public Health and Safety

Titmuss's claim that VNRD plays an essential role in minimizing risk to public health has been called into question, though public, professional, and political support for the maintenance of VNBD remains high. Support for VNRD is evident in existent literature on the geography of plasma collection facilities. Most of this work emphasizes safety concerns stemming from donor populations, and argues, like Titmuss, that clinics disproportionately locate in impoverished and minority communities, and that these practices compromise safety of the blood supply. The logic is that such populations are likely to be desperate to the point of misrepresenting their medical/risk history in order to ensure they can donate and get paid.

Most of the medical literature concerned with safety has focused on potential communication of diseases through the contaminations of blood and plasma products. However, there have been continuous improvements to the safety protocols of blood systems in developed countries. Currently blood products are tested and treated for historically problematic viruses. But there remains concern regarding the emergence of unknown transfusion transmitted infections (TTI) unaccounted for by current safety measures (Franchini 2010; Dunn and Young 2018).

The fear of this risk still resonates because of the blood and plasma communicated HIV outbreaks of the 1970s and 1980s. During this period approximately 63% of American hemophiliacs had been infected with HIV. The rate was much higher (96%) for those suffering from severe hemophilia, which requires regular use of factor VIII, a concentrated clotting agent commonly used by hemophiliacs. The World Federation of Hemophilia reported in 2001 that among the global hemophiliac population at that time, about half were infected with HCV and about 10% with HIV (James 2003). However, advancements in testing and material treatment

now form layers of precautions and have dramatically decreased instances of viral infection through transfusion (White 2010; Weinstein 2018). White (2010) noted that because of pasteurization and viral detergent inactivation of factor VIII, there were essentially no new cases of factor VIII-implicated HIV-1 after 1985 (see also Franchini 2010).

There are also potential risks for individual donors. Plasma donors must be 18 years of age and weigh at least 110 pounds. All individuals must pass a medical examination, medical history screening, and testing for transmissible viruses before their donation can be used for manufacturing. The FDA maintains that blood and plasma donations are safe, but there are noted associated risks (Hendrickson and Hillyer 2009). Plasma loss is potentially medically significant and may contribute to increased heart rate, drop in blood pressure, hemoconcentration associated risks like hypercoagulability, and hypovolemic shock. There is also the risk of death. Annualized rates from 2005 – 2011 for reported fatalities following source plasma donation ranged from 1.0 to 8.5 fatalities per ten million donations (Williams 2013). It has also been argued that little is known about long term effects of frequent plasma donation (Shaefer and Ochoa 2018), which may also interact with other social determinants of health.

The scant literature concerning clinic location has explored its link with public health and safety. To date, James and Mustard's (2004) is the only geographic survey/analysis of plasmapheresis clinics in the US. Over the 1980 - 1995 period they examined the location of commercial plasmapheresis clinics in the United States and their spatial relationship to the distribution of risky behaviors associated with TTIs. Their motivation was to test the "Chitwood Assertion" (James 2003, 201), that "commercial blood centers often are located in inner-city neighborhoods where poverty and drug use are prevalent" (Chitwood et al. 1991, 632).

James and Mustard (2004) noted while numerous sources and anecdotal reports had speculated that paid blood and plasma were overrepresented in economically disadvantaged areas

(for examples see Kretzmann 1992; Volkow 1997; Carney 2011; Weimer 2014; Edin and Shaefer 2015; 2018), theirs was the first empirical analysis of commercial plasmapheresis centers and their geographic organization. James and Mustard (2004) concluded that commercial source plasma clinics were overrepresented in neighborhoods with active local drug economies and, that these locating practices continued after the links between HIV and HVC infections and plasma products had been established.

Volkow et al. (2009) studied the circumstances surrounding paid plasma donation among intravenous drug users (IDUs) in two Mexico–U.S. border cities, and found that while plasma selling appeared rare in the cohort, paid donations from previous IDUs had occurred well after the 1980s safety reforms had been established. Inspection for injection stigmata is embedded in clinics' Donor History Questionnaire, suggesting donors had concealed their risk status. The authors emphasized paid donation as a matter of public inquiry and noted the limitations of deferring donors based on behavioral risks (see also Penrod et al. 2010; Volkow et al. 2010).

Existent research into the geography of plasma collection has two major limitations. First, this work has suffered from constraints in research methodologies. Titmuss's work, in some respects, was poorly executed, but he faced data limitations and a lack of guidance from any antecedent research. Work conducted by medical and public health professionals (e.g., those noted above) is often limited to case studies because their methods are time and resource intensive (e.g., collecting surveys of donors' complete medical history, and antibody testing). Second, exclusive focus on public health policy has come at the expense of exploring the geography of blood plasma through other topical lenses. Apart from vital public health policy applications, clinic locations may speak to important social and ethical concerns, particularly the pitfalls of a reliance on market rationale in every aspect of life.

US Plasma Collection, Geography, and Ethics

Compensated plasma collection, like other bodily commodifying practices, raises ethical questions about social justice and exploitation (Titmuss 1971; Kretzmann 1992; Farrugia, Penrod, and Bult 2010; Sandel 2012; Shearmur 2014; Weimer 2014; White 2014). Moral philosophers and ethicists engagement with bodily commodification, especially its more extreme forms (e.g., organ markets), is well trod. However, contemporary discussions of commodified plasma have only been hashed out in less academic forums (Edin and Shaefer 2015; Nord 2016; Shaefer and Ochoa 2018). Industry representatives have repeatedly pushed back against claims of exploitation especially the suggestion that the US model has contributed to the development of a permanent donor class. Arguments from industry range widely - from their inability to act against a systemic problem, to outright denial (Farrugia, Penrod, and Bult 2010; Penrod et al. 2010). Industry representatives have at times also been hesitant to generally discuss the ethics of commodified plasma (Shaefer and Ochoa 2018).

Information on locating practices is not publicized. It is likely that siting decisions are proprietary and important to industry competition. Equally likely, is that public knowledge of input variables in such decisions could potentially cause a public relations backlash, if accusations of targeting certain communities were confirmed. The geography of clinics is an important component in the ethical discourse of plasma collection. But critics often cite anecdotes because of a lack of a comprehensive geographical analysis. The absence of this critical information highlights the fact that there is a spatial dimension to nearly every injustice. Further, it demonstrates that geographers are well placed to uncover injustices because of their unique interest in, and skills to, explore how and why spatial relationships originate and evolve (Carmalt 2018; Ozias and Pasque 2018).

The aim of this research is to inform ethical arguments concerning commodified plasma in the US through geographic analysis. In particular, the dialogue between industry representatives and their critics is addressed because there seems to be significant disagreement about clinic locating practices and donor constitution. Empirically demonstrating the geographic patterns of socio-economic characteristics in relation to clinic location would aid in the developing ethical discussions.

Critical GIS, Landscapes of Predation, and Locational Logic

This work draws upon aspects of the critical GIS tradition and Graves' (2003) concept of predatory landscapes, both of which highlight practical and ethical approaches to the production of geographic knowledge and the consequences of its use. Critical GIS is situated in geography's broader critical tradition which reflects a diverse set of literatures encompassing multiple theories (Castree 2000; Blomley 2006). Blomley's (2006) reading of critical geography describes it as oppositional to inequality or oppression, with a core goal of changing the world through practical and reflexive approaches informed with the insights of social theory. It is also worth noting Blomley described critical geography as generally skeptical of quantitative and positivist approaches. The notion that critical geography is incompatible with such approaches is rejected here (Barnes 2009; Kwan and Schwanen 2009; Wyly 2009). For example, synthesizing the rigors of GIscience with social theory has produced meaningful insights into fields formally considered antiquated and devoid of theory – toponomy and electoral geography (Webster, Chapman, and Leib 2010; Warf and Leib 2011; Fuchs 2015; Caturia 2018; Chloupek 2018; Kinsella, McTague, and Raleigh 2018; Oto-Peralías 2018; Reid and Liu 2019). Conversely, the historically positivist or quantitative oriented subfields of physical geography have recently incorporated aspects of social theory (Carey et al. 2016; Kelley et al. 2018).

Crampton (2010) suggests critical GIS and critical mapping typically fall into one of four overlapping strands of thought. The first strand includes the acknowledgement of important contributions made by GIScience in terms of its ability to organize and produce knowledge about the world. Simultaneously these contributions carry and rely on certain assumptions that can, and often do, go unscrutinized. The second strand includes the use of historicization and spatialization of knowledge production as a way of challenging assumptions that may be 'cooked into' mapping practices. The third strand recognizes that mapping and geographic knowledge, to the extent that it is influenced by social, economic, and historical forces, is inherently linked to power/politics. The final stand of critical GIS necessarily has an "emancipatory flavor to it." Critical mapping often aims to disrupt official knowledge. Challenges may take the form of hypothesis testing of official knowledges and highlighting misrepresentation. They may also come by way of giving cartographic voice to those ignored in official discourses.

This research works mostly within the last strands by engaging official spatial knowledges produced and reinforced by corporate interests. Official spatial knowledge is rarely corporate alone, as it is also part of the broader political-economy that permeates the political, economic, and social. As such it carries ethical implications (Goodwin 2004). This was recognized early on by Pickles (1995) in his presentation of GIS's implication in the service of corporate and state interests to facilitate surveillance and control, and mask social and economic inequality.

Official knowledge and discourses are constructed by what is stated, but also by what is withheld. As noted above the official knowledge on clinic location is characterized by avoidance. There are certainly logics guiding locating practices – to ignore the importance of location in an increasingly lucrative industry makes little sense. Even if companies would not disclose for competitive purposes there are other ways to address ethical criticism of targeting the poor.

Companies collect donor data and have released it to industry friendly trade organizations for analysis, but racial and income data is either not collected or withheld.

Along with theoretical guidance from the critical GIS tradition, the paper also draws upon Grave's (2004) landscapes of predation, a term to describe the spatial targeting of disenfranchised neighborhoods by fringe financial services. Subsequent work has confirmed and expounded upon Grave's inquiry, including the importance of community characteristics like class, occupation, race/ethnicity, nativity, age, and military affiliation in affecting the likelihood of hosting fringe services (Gallmeyer and Roberts 2009; Crossney 2010; Peterson and Graves 2010; Cover, Spring, and Kleit 2011).

Grave's (2004) concept serves as a guide for a few reasons. First, because of similarities in approach, it lends guidance for methodologies and perspectives on economic critiques. Second, the concept involves a dialogue also reflected in the plasma collection economy. There are similar discourses emanating from both industries. In the case of plasma collection, criticisms of locating practices are denied, ignored, or framed in neoliberal terms, evoking client/donor freedom or consumer/patient centeredness. Similarly, the fringe banking industry accounts for their location practices by arguing that they fill a void left by traditional banking services.

Third, the concept seems to describe an ecosystem or "social ecology" (Gallmeyer and Roberts 2009, 522) shared by both industries, with the proliferation of each occurring against the backdrop of growing economic insecurity. This link is evident in the opening of Graves' (2003, 303) in which he describes the new signifiers of American urban poverty

> . . . among them deferred deposit lenders, popularly known as "payday lenders." In recent years, these and other sources of quick cash have begun to mark the boundaries of tough neighborhoods, vying for space among other emergent signifiers of poverty, such as rent-to-own appliance stores and plasma collection centers

Finally, Grave's (2004) landscapes of predation, in the context of fringe banking, serves as an illuminating contrast to explore plasma collection's own predatory landscapes. An important difference is the nexus of supply, demand, and exchange in each industry. Arguably the locations of fringe banking services reflect the meeting of consumer demand. Since fringe entities do not provide savings services the exchange interface between service provider and customer is straightforward. But exchanges in plasma collection disrupts this understanding. It is unclear which is customer, and which is the service provider.

There are differing conceptions of both donors and recipient of plasma in The Source, a magazine publication of the plasma protein therapeutics industry (see Chapter 2). The Source is published by the Plasma Protein Therapeutics Association, a trade association representing the private sector's interests of the biologics and biotechnology industry. In that publication donors have been described as the cornerstone of the industry, and their plasma as a "precious starting material." Donor contact with clinics have also been described in terms of *customer* service experience. Similarly, recipients of manufactured products are referred to as patients, consumers, the forgotten, and stakeholders.

Additionally, disruption of exchange norms is evident in the geography of demand. Most economic exchanges occur at the co-location of supply and demand, but demand driving the increase of US plasmapheresis clinics is not local. The demand for plasma is distant and displaced by export-based profits and is driven by consumption from abroad. This suggest that rather than a von Thunen-like nexus of willing buyers and sellers, it may be more appropriate to think about clinic locations in Weberian terms with donors conceptualize as a relatively fixed natural resource.

However, neither of the geographically informed von-Thunen or Weberian theories necessarily fit within the predominate policy debate over blood and plasma because they are both

purely economic theoretical models. In contrast, the primary debate associated with blood and plasma features is not purely economic. The two opposing views revolve around whether blood should be viewed as a gift or a commodity (colloquially known as the 'gift versus commodity debate'). This debate became entrenched with concerns over donor exploitation and higher rates of TTIs, which accompanied the global development and expansion of the for-profit industry from the late 1960s onwards (Farrell 2006). NGOs and national blood services continue to support VNRD as echoed by Titmuss's conception of the gift relationship. The opposing side favors compensation-based models. Support for this commodity-conception largely emanates from the for-profit industry. Farrell (2012, 14) describes the debate as a reflection of tension between "the social and the economic" created by rapid capitalist market expansion and technological innovations in the bio-economy. Her critique of the dichotomous framing highlights its practical deficiency in both risk management of national blood systems and understanding international market forces.

The 'gift versus commodity' dichotomy potentially also falls short in ethical debates. Farrell (2012) notes that the two sides of the dichotomy reflect ethical components with "deeper and more complex roots in notions of reciprocity and exchange, as well as property and control," but non-profit representatives' invocation of "the gift" as a defense of VNRD was closely entangled with concerns with contamination risk, not ethics. After HIV blood contamination episodes in VNRB-based national systems, the debate was further complicated because safety was no longer tied to the gift conceptions ethical concerns. This revealed that ethics were probably not a major component of the debate separate from other concerns. This work can potentially compliment dichotomous framing as it applies to ethical discussion because the focus is primarily on exploitation rather than public health and risk.

Data and Methods

The locations of for-profit plasmapheresis clinics were collected through a Freedom of Information Act (FOIA) requests of FDA blood establishment registration records. The FDA requires establishments that engage in the manufacture of biologic products to register and list products with the agency. Clinic data from years 2004-2006, 2009-2011, 2015 were requested. Clinic data from 2017 were collected manually from the FDA's blood establishment database on 3/16/17. FOIA data were received as photocopied registration forms. Preparation of clinic location data was conducted in three steps. First, the form PDFs were manually filtered by establishment type with only those marked as plasmapheresis center selected. Forms were then filtered by ownership type. Only records for firms owned by for-profit corporations, partnerships, or single proprietors were retained. Finally, clinic addresses were collected from registration forms and geo-located.

Locational data of clinics, along with Census and American Community Survey data, were analyzed for spatial-autocorrelation. Block group level socio-economic variables included eligible donor proportions by age, racial and ethnic proportions, and median household income. Variable selection was informed by previous research and journalistic reporting that has suggested overrepresentation of clinics in poor minority communities. Results were further scrutinized at a finer scale in select metropolitan areas.

Similar studies analyzing fringe firm proximity have not been national in scope, with the exception of Fowler et al (2014) who used counties as observational units. Subcounty scale analysis is appropriate for fringe financial activity because of high volume. For instance, Cover et al (2011) reported 117 fringe firms in the Boise ID metro area alone. However, because of the smaller number of plasma clinics and their wide distribution across the US, a national survey

using block groups as observational units was preferred, as they provide a more focused measure than either census tracts or zip codes (Gallmeyer and Roberts 2009).

This approach is similar to James and Mustard's (2004) national survey, but differs by use of a finer scale observation unit and the combination of analytical methods. James and Mustard (2004) used census tracts and binomial analysis to measure the difference in clinic presence and absence. Building upon this, block groups are utilized which are a common proxy for neighborhoods and provide additional granularity than census tracts (Gallmeyer and Roberts 2009). Tracts can also vary substantially in terms of area and socio-demographic constitution. Binomial based analysis with optimized hot spot analysis (HSA) is also combined. HSA allows for exploration of spatial structures defined by the data, requiring less reliance on the structure of the predefined observational units.

Analysis

The analysis was conducted in three steps. First, socio-economic data were summarized by calculating the mean values with respect to their relationship to clinics. Block groups (BG) were categorized as inside or outside a seven-mile buffer of a single clinic. This provided comparable mean values – e.g., the mean poverty proportions of all BGs outside of a buffer could be compared to the mean poverty proportions of all BGs inside of the buffer. Next, to confirm the pattern suggested by the descriptive statistics, variables of the two groups were compared for statistical significance using an independent t-test.

Finally, the analysis was focused by applying an optimized hot-spot analysis on two intra-state cases. HSA is a form of cluster analysis widely used in geography, public health, criminology, ecology, and many other fields as an exploratory technique. Clustering phenomena can be important to understanding spatial structures or mechanism attributable to place and local contexts (Grubesic, Wei, and Murray 2014). HSA creates a map of statistically significant hot and

cold spots as determined by a selected feature attribute. The HSA tool produces z-scores and p-values for each feature in a dataset by calculating the Getis-Ord Gi* statistic. Each feature is evaluated within the context of neighboring features. To be a statistically significant hot spot, a feature must have a high value and be surrounded by other features with high values. Local sums for a feature and its neighbors are compared proportionally to the sum of all features. When the observed local sum is different from the expected value, and when that difference is too large to be attributable to chance, a statistically significant z-score results.

National level data were entered into a series of HSAs and subsequent results were mapped for a fine scale cartographic analysis. National data were used because limiting the HSA calculations to the two state case studies would introduce bias and reflect only relative hot-spots within the state. Theoretically, clinics could be placed anywhere in the US. Given this assumption, all BGs are relevant features to the analysis.

Before discussing the results, it is worth noting the limitations of the analysis. The methods used here are fairly conservative. Both the T-test and HSA do not consider variation in importance of individual block groups. For instance, there is no distinction between block groups falling within the 7 miles of one or multiple clinics. Second, the HSA may potentially masks instances of clinics location in poor neighborhoods if there is insufficient clustering or prevailing conditions. For example, if poverty is highly concentrated and stark in comparison with neighboring wealthy areas it could be washed out in the analysis.

Additionally, the model cannot capture all the complexities inherent in firm locations. Donor populations are only one factor in determining clinic location, albeit a substantial one. Ultimately these firms are committed to profit generation, thus future research should consider other factors potentially affecting the bottom lines of firms. Literature focused on fringe economic activities noted the importance of factors like state regulations and indirect market

forces (Cover, Spring, and Kleit 2011; Fowler, Cover, and Kleit 2014). Similarly, factors important to clinic location might include the cost of commercial land/rent, the presence of a semi-skilled labor pool to work as phlebotomists, and local zoning restrictions. Variables related to accessibility would likely need to be incorporated. Accessibility, depending on the area, might reflect car ownership or public transit access. Cities are not spatially uniform in terms of connectivity or accessibility, and it seems likely that companies would consider this when determining location. Urban level analysis of public transportation would likely explain some of the intra-urban variation in clinic locations.

Results and Discussion

The summarization of block group data indicates that on average block groups near clinics tend to have higher proportions of racial and ethnic minorities, and higher rates of poverty. Additionally, this pattern of difference is consistent over time. The observed patterns were confirmed by independent t-tests of 2017 clinics. Additionally, population proportions of eligible donors (18 years or older) within seven miles of a clinic were smaller than those beyond seven miles of a clinic. This suggest the quantity of eligible donors may be less important to determining clinic locations than other qualitative characteristic like poverty, race, and ethnicity.

It is worth noting that despite similar means the difference between BGs proportion of eligible donors were still statistically significant. This may be attributable to the number of observations entered into the statistical test. As suggested by Warf (2011) large sample sizes can lead to misleading coefficient significance in standard statistical testing of global datasets (see also Faber and Fonseca 2014; Kaplan, Chambers, and Glasgow 2014). Further, Warf notes that simple bivariate tests can disguise as much as they reveal because variables like race and class can be intertwined in complex ways, and the importance of a single variable can vary across space.

The HSA provided a method of finer scale evaluation for two state level cases. Texas and Utah were selected because they had the most clinics and most clinics per capita, respectively in 2017. Most of the target variables selected for the series of HSAs included those used in the t-test. Because the measurement of poverty does not take into account geographic differences of living costs, median household income was substituted. Finally, only appropriate HSA maps are reported below. For instance, the HSA of black proportions in Utah provides little information because the state's overall proportion is about 1%. Thus, there are no hotspots, or cleavages, of black population proportions capture in the analysis.

Utah

In general, the results suggest that firm locations reflect a mixed profile. A majority of Utah's clinic are concentrated along the Wasatch Front. Most of these clinics were concentrated in Hispanic communities or ethnic transitional areas (Figures 3 and 4), with the exception of the few clinics found in Southern Utah.

Figure 1. Optimized Hotspot Analysis of Hispanic Proportions in Northern Utah

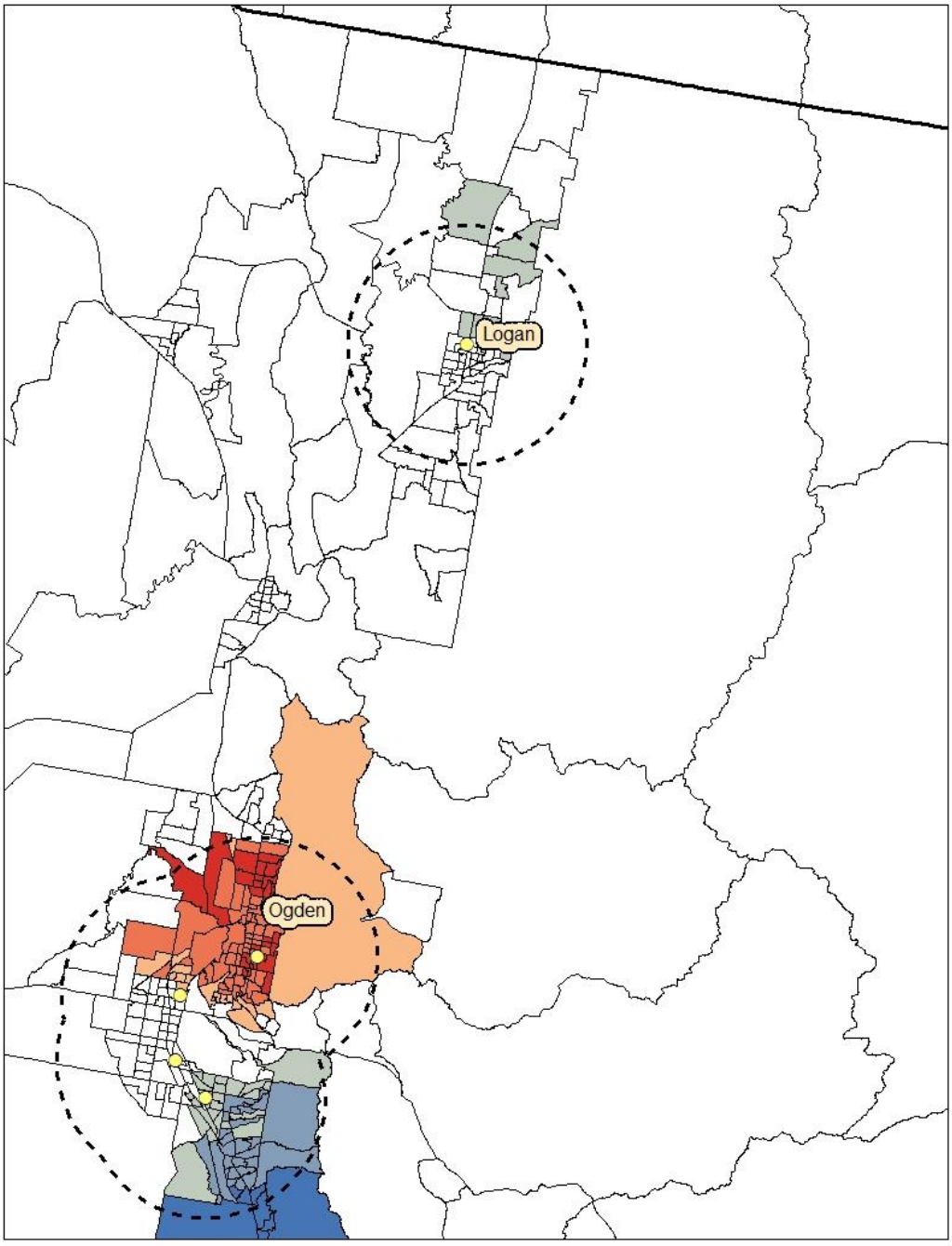
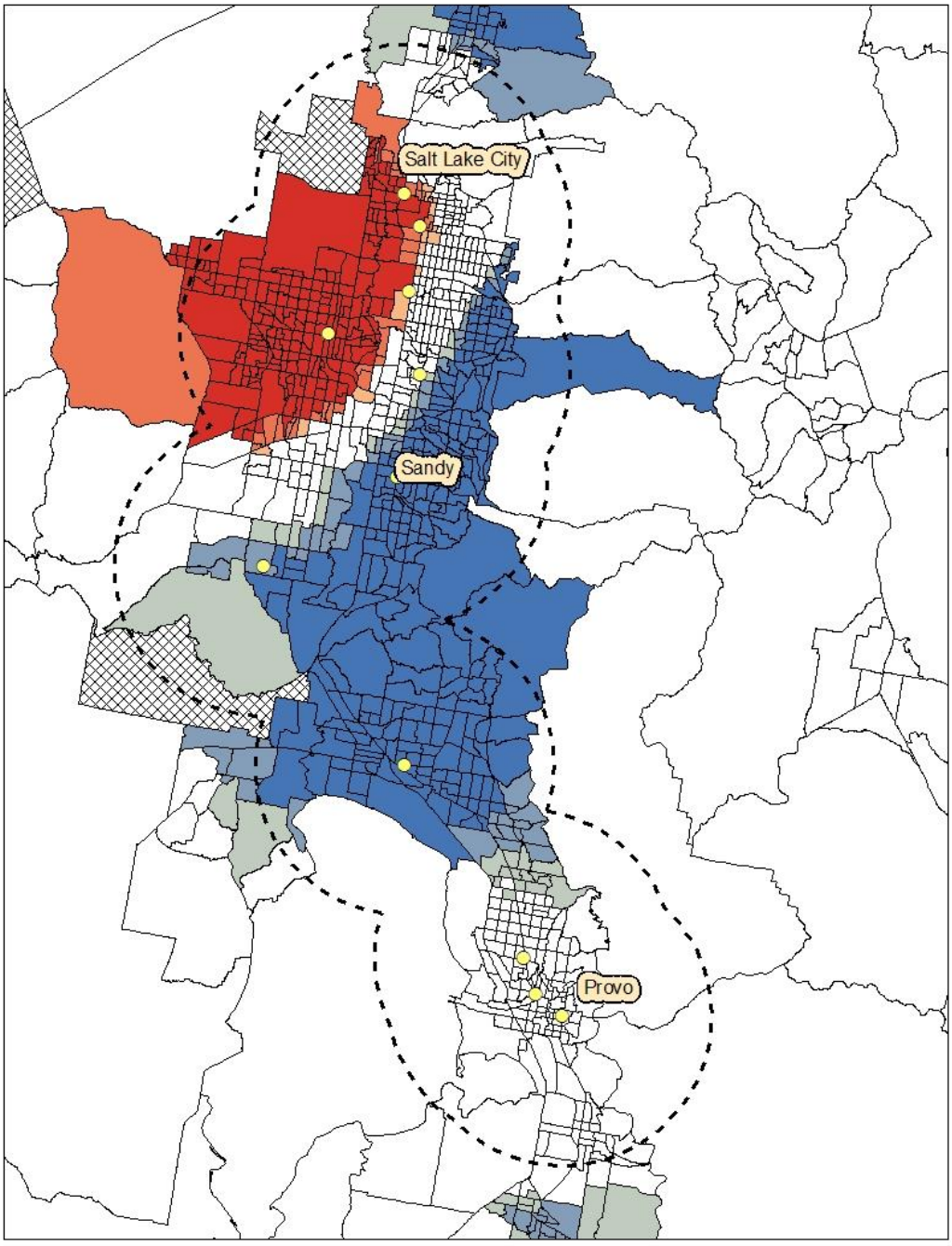


Figure 2. Optimized Hotspot Analysis of Hispanic Proportions in Salt Lake City



Most, but not all clinics were near spatially concentrated low-income values (Figures 5-7). Two clinics in south central Salt Lake County were in the middle of a high-income hot spot.

Interestingly only four clinics were located near clustering high proportions of eligible donors. All of these clinics were located in central Salt Lake City, adjacent to the University of Utah (figures 8-10). A majority of clinics throughout the state were near four-year universities. Finally, all clinics locations were within 7 miles of clustering cores of lower income or higher racial and ethnic minorities (15 of 19), or 7 miles of the respective cleavages.

Figure 3. Optimized Hotspot Analysis of Median Household Income in Northern Utah

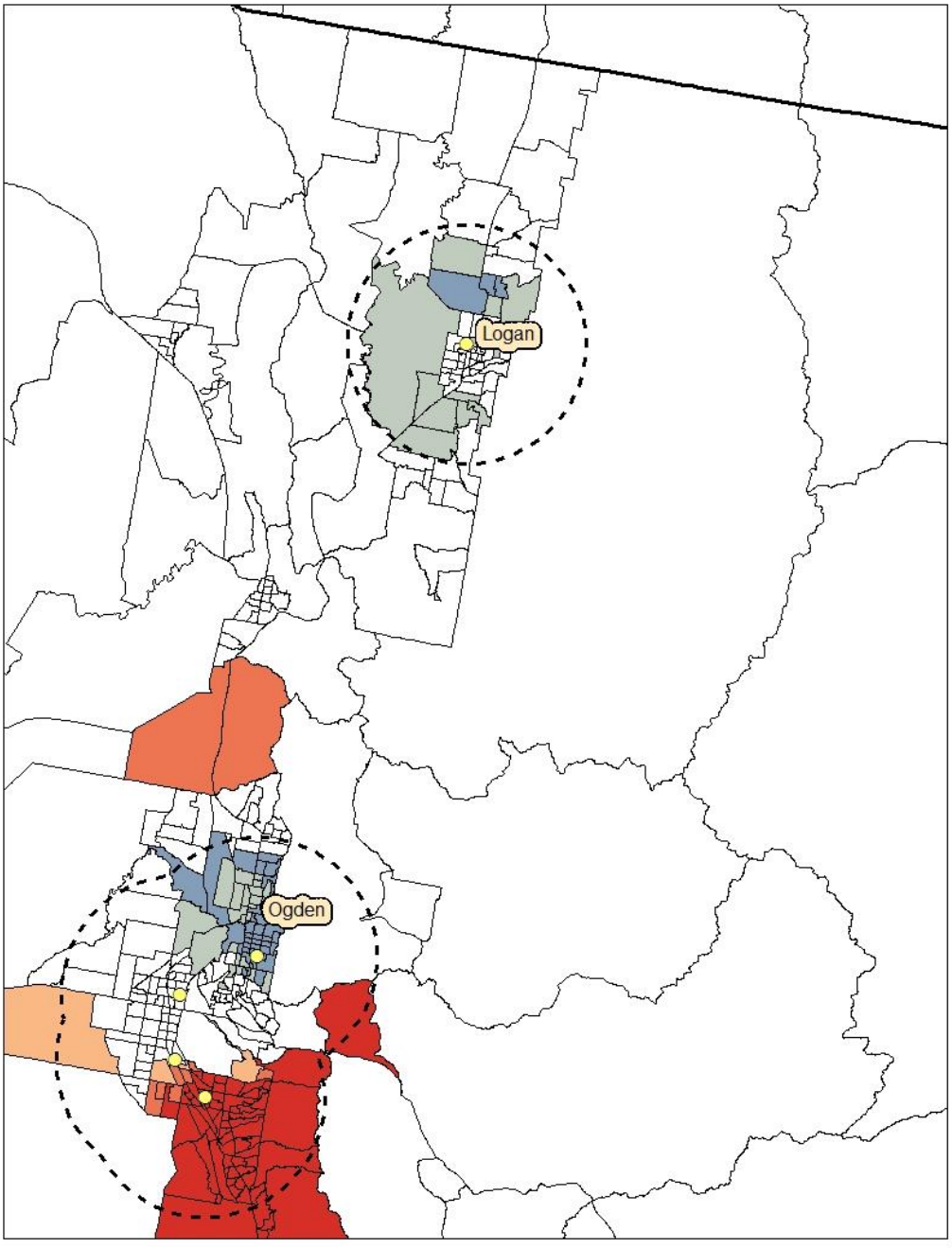


Figure 4. Optimized Hotspot Analysis of Median Household Income in Salt Lake City

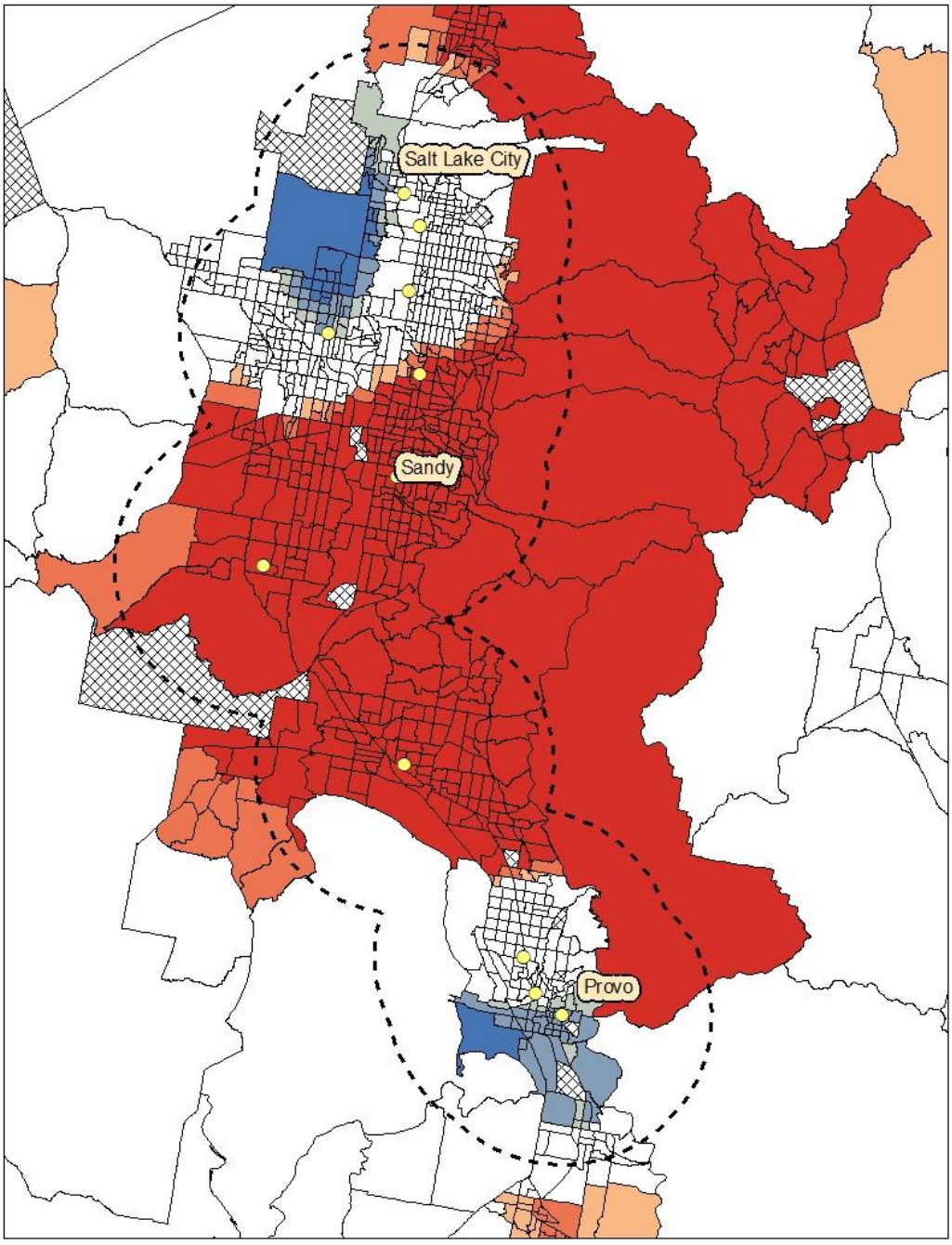


Figure 5. Optimized Hotspot Analysis of Median Household Income in Southern Utah

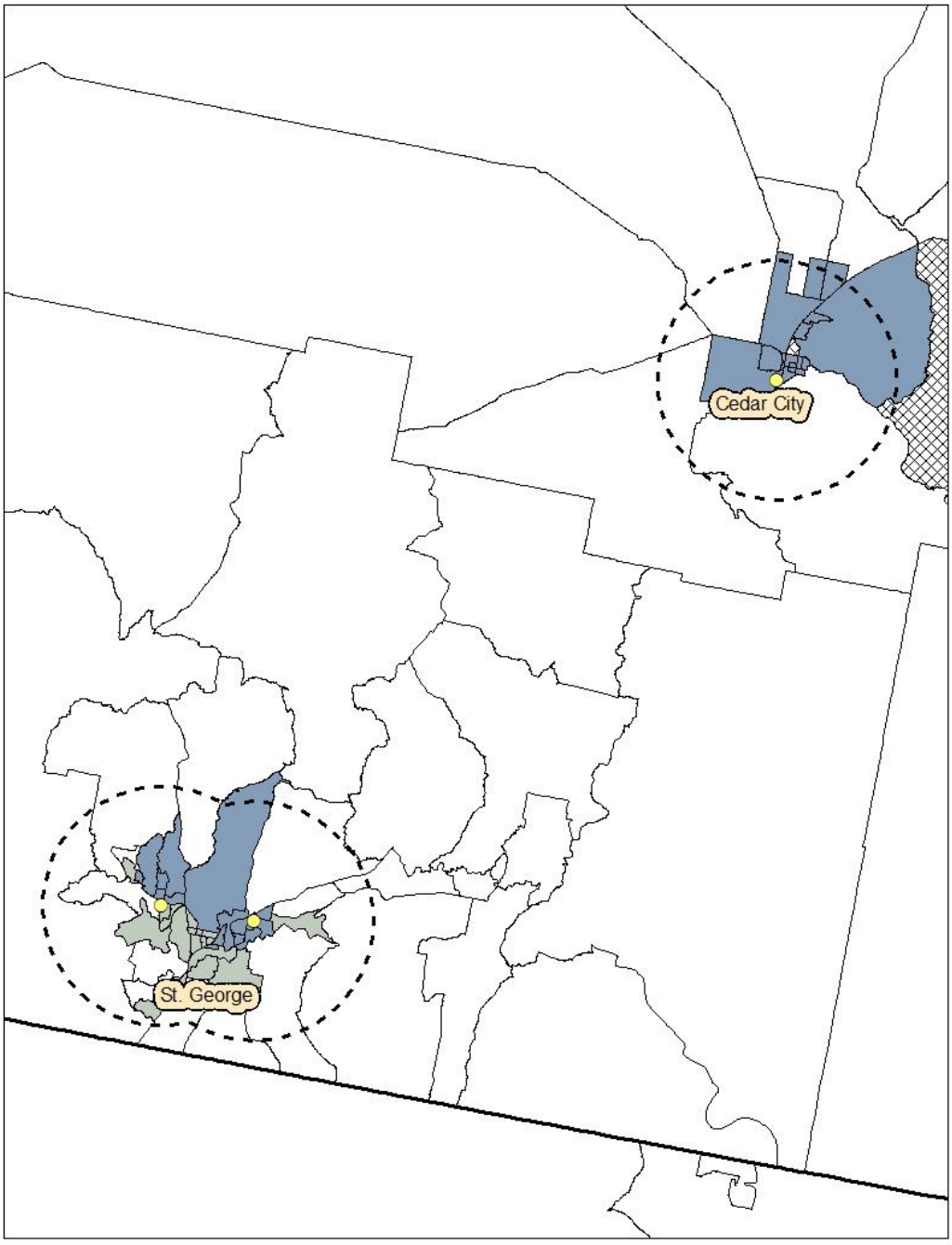


Figure 6. Optimized Hotspot Analysis of Student Proportions in Northern Utah

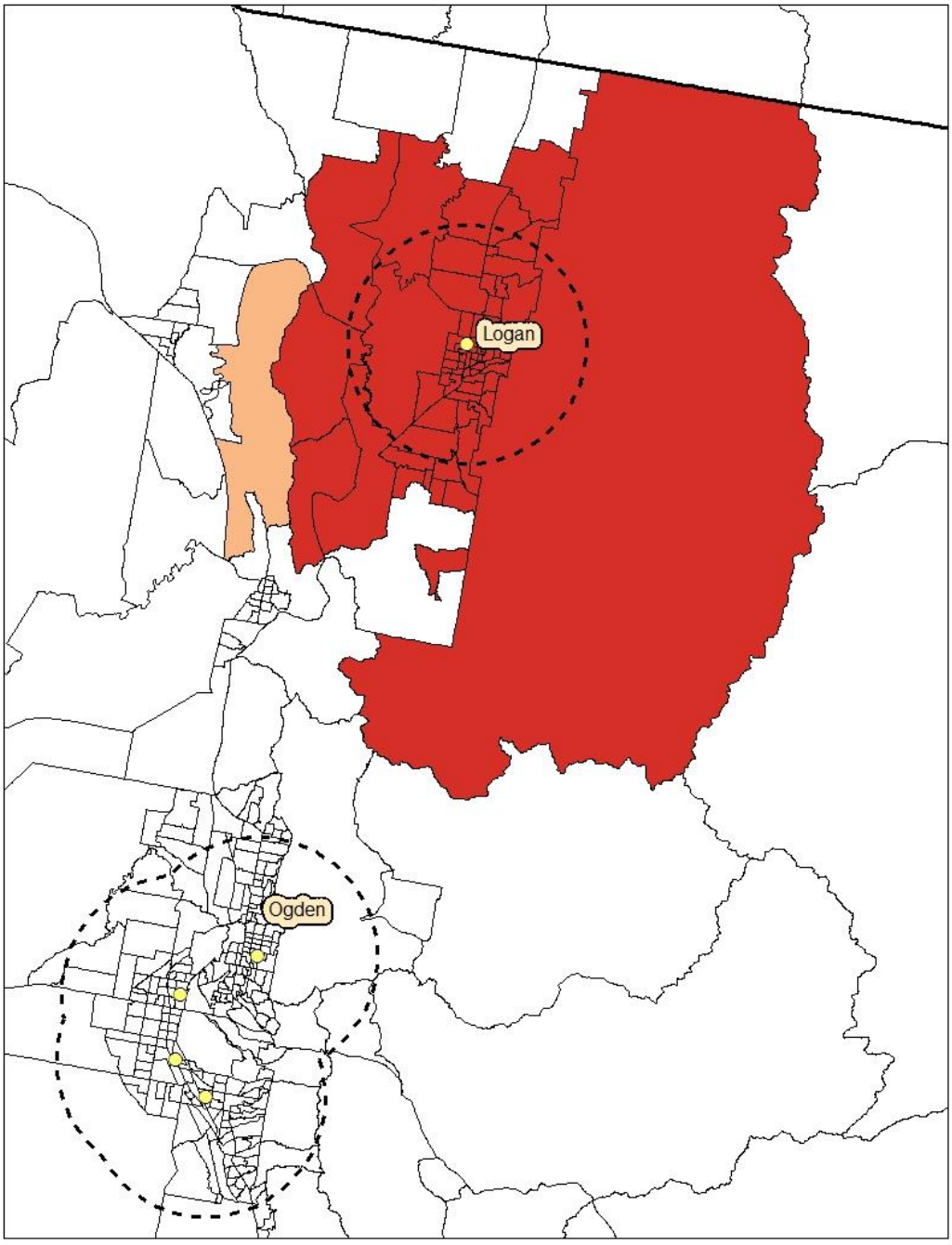


Figure 7. Optimized Hotspot Analysis of Student Proportions in Salt Lake City

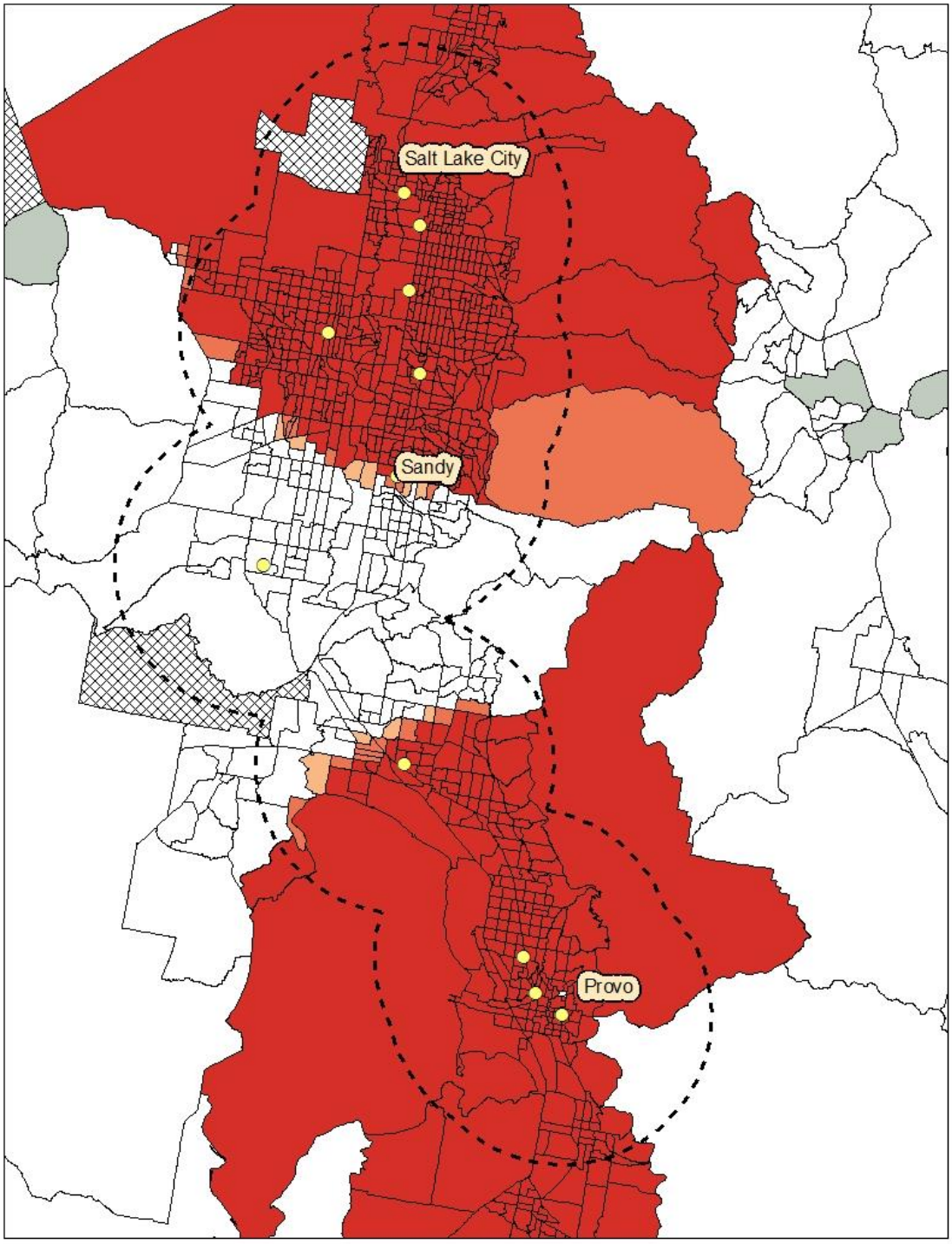
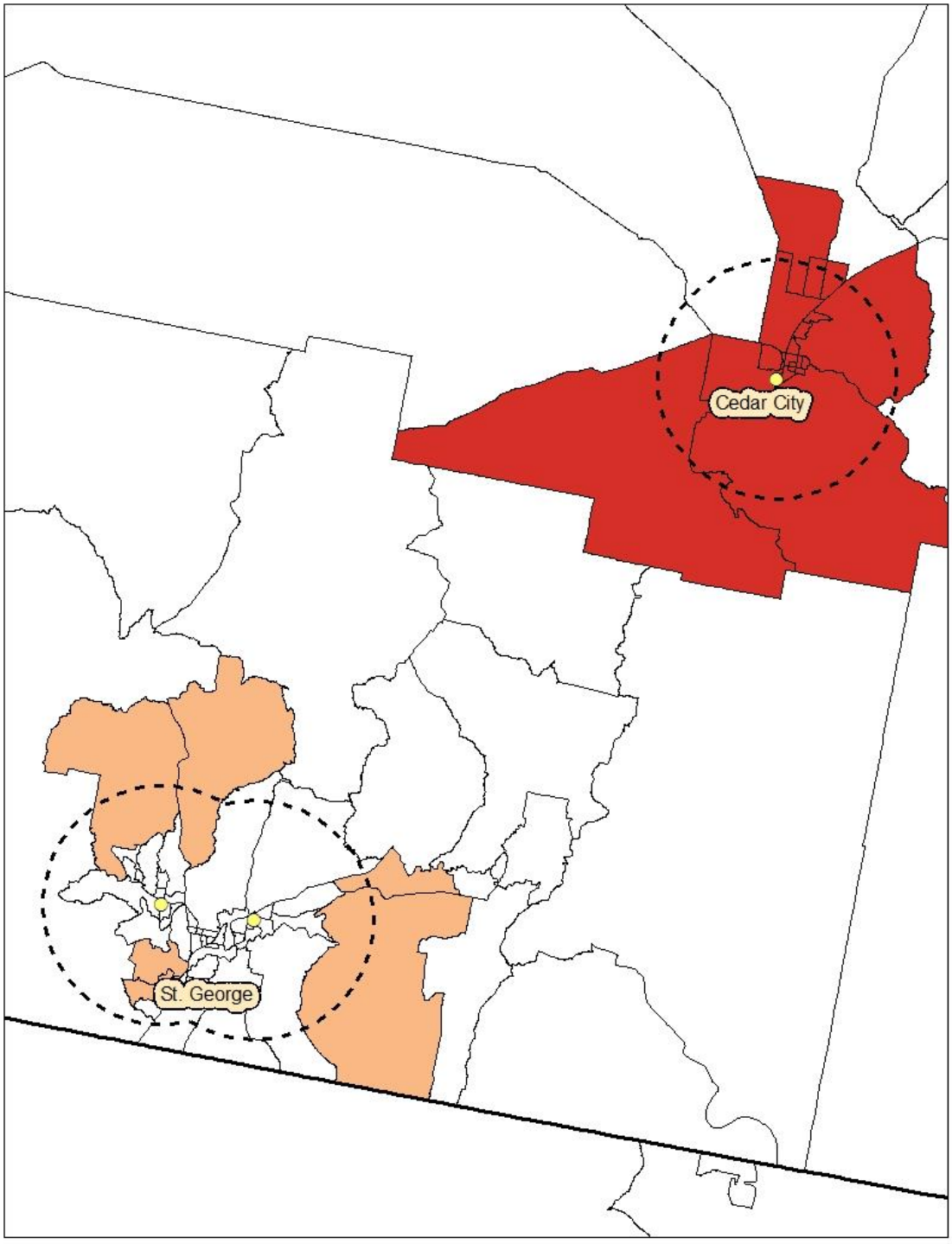


Figure 8. Optimized Hotspot Analysis of Student Proportions in Southern Utah



Texas

Texas provides a good contrast from Utah because of its racial and ethnic diversity. Utah's primary demographic distinction is between Hispanic (13%) and Anglo (86%) residents. Texas's residential make up is roughly 43% Anglo and includes a sizeable proportion of both black (11.8%) and Hispanic (39%) residents. San Antonio, Dallas-Fort Worth, and Houston contained the largest collections of clinics. Income cleavages were more clearly developed in these cities than in parts of Utah (Figures 11-13). And in a majority of instances clinics fell completely inside income-based cold spots. The remaining clinics, while not entirely within cold spots, were in areas of hot/cold transition.

Figure 9. Optimized Hotspot Analysis of Income in San Antonio

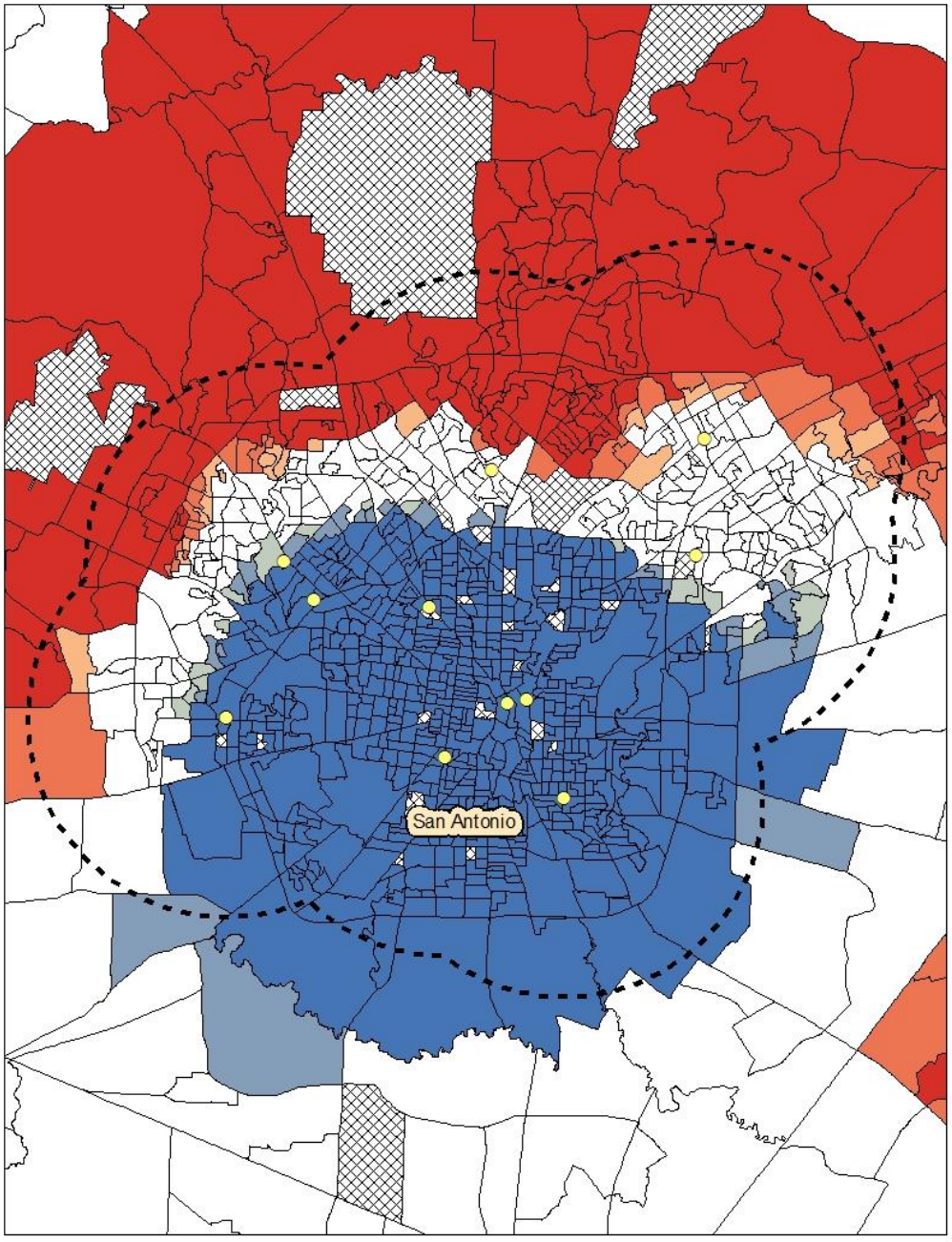


Figure 10. Optimized Hotspot Analysis of Income in Houston

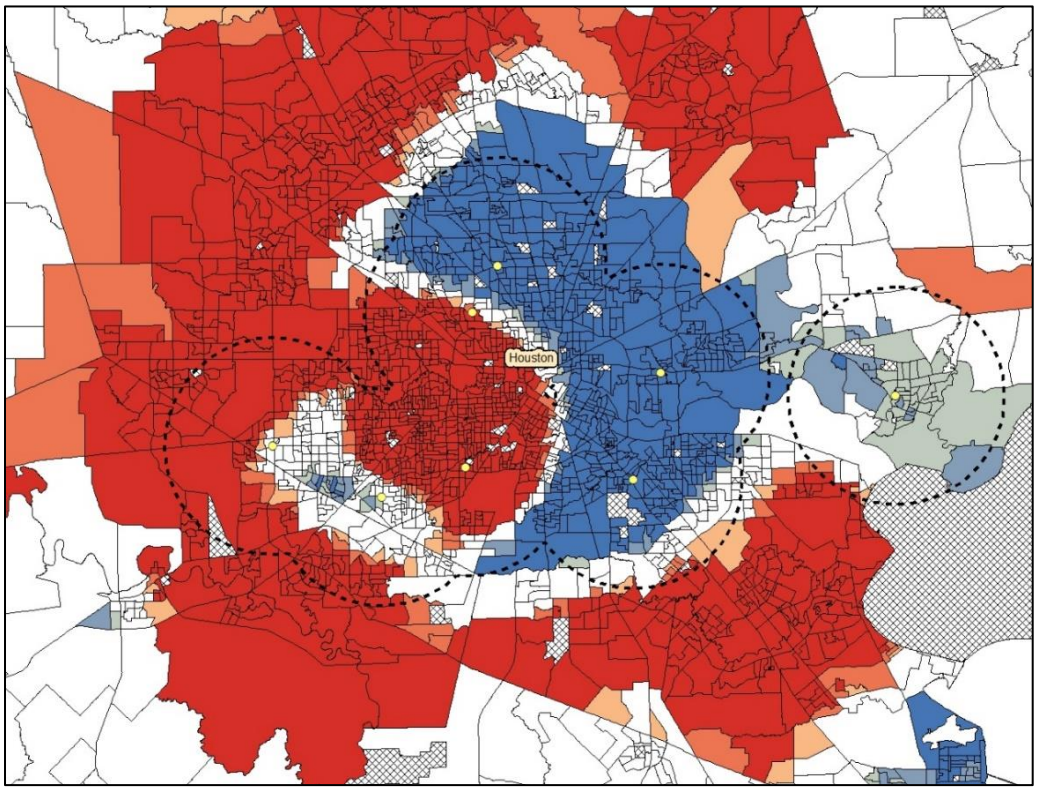


Figure 11. Optimized Hotspot Analysis of Income in Dallas-Fort Worth

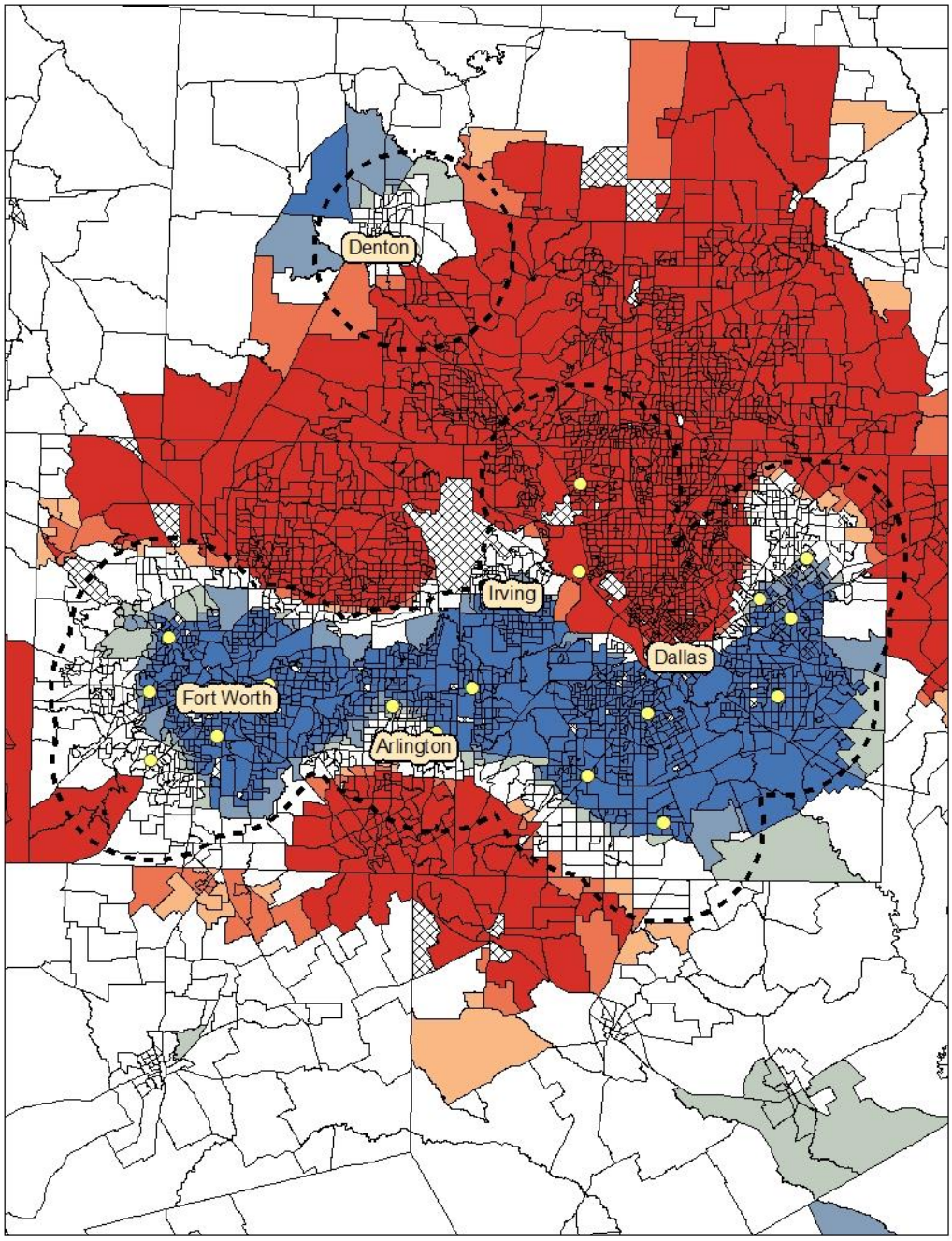


Figure 12. Optimized Hotspot Analysis of Anglo Proportions in Dallas-Fort Worth

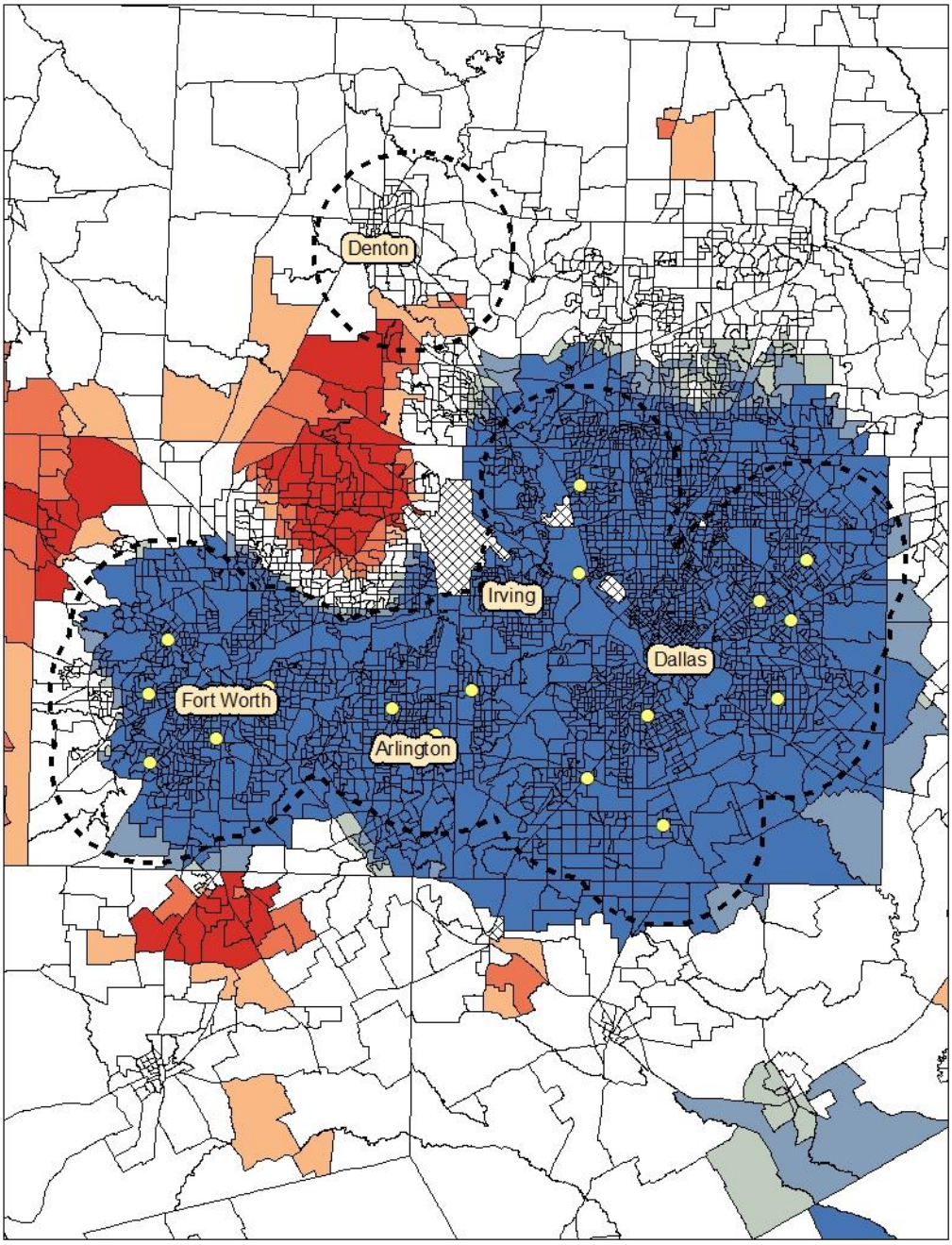


Figure 13. Optimized Hotspot Analysis of Black Proportions in Dallas-Fort Worth

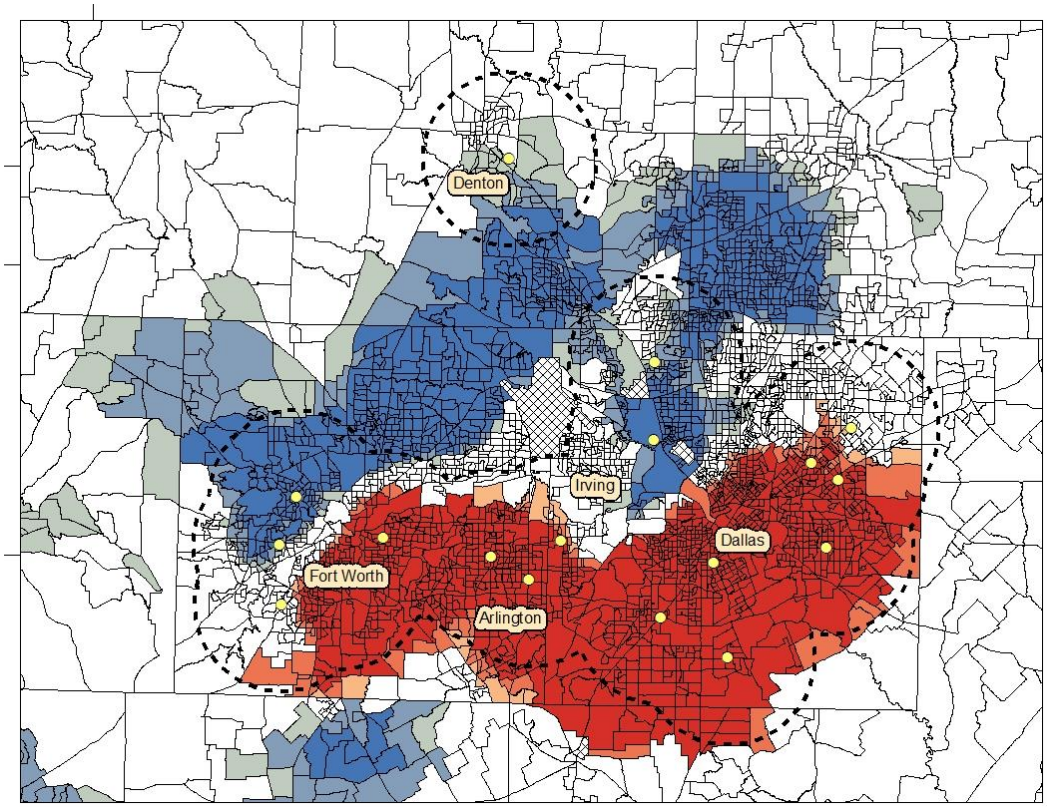
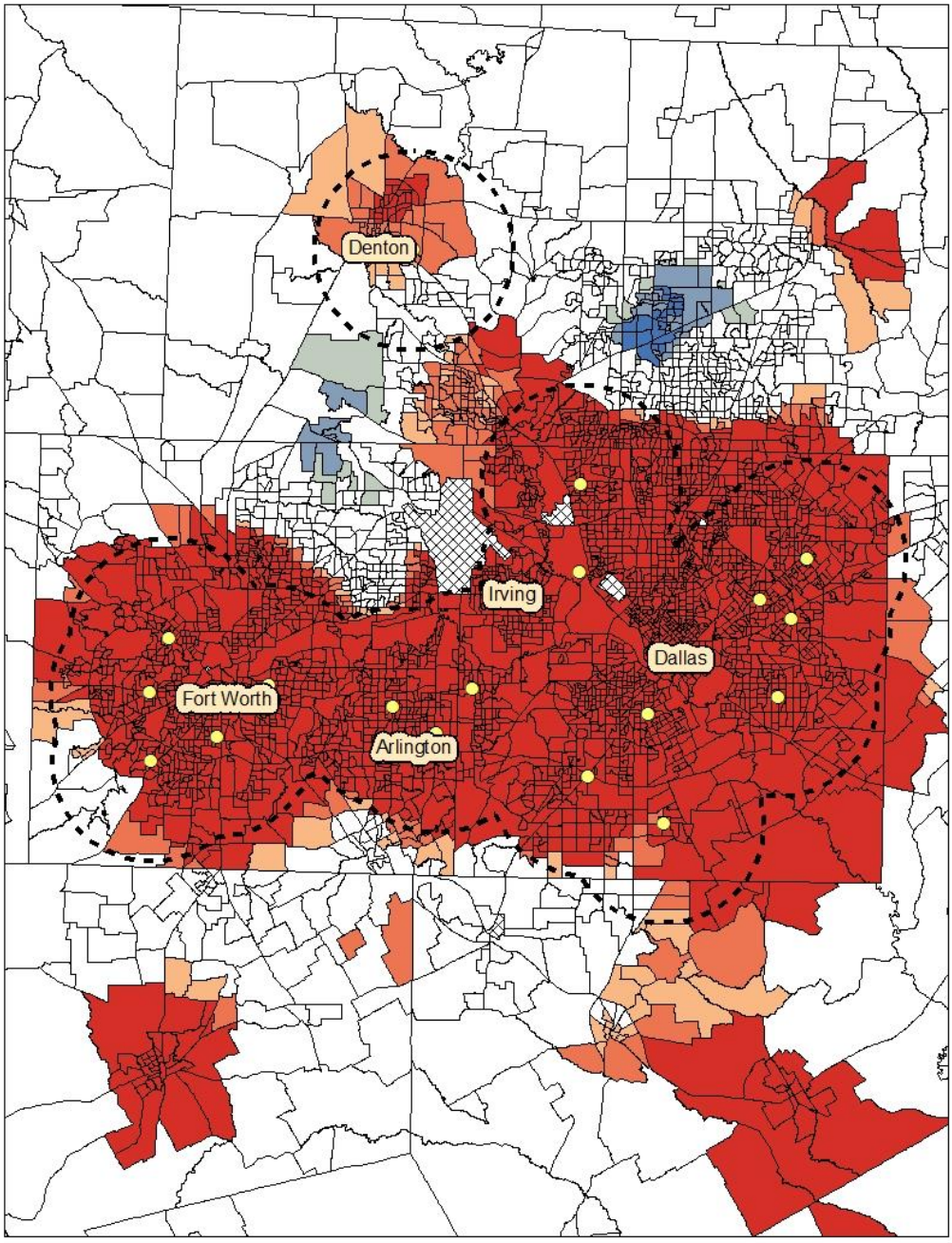


Figure 14. Optimized Hotspot Analysis of Hispanic Proportions in Dallas-Fort Worth



Race and Ethnicity

Hot spot analysis of racial and ethnic proportions in Texas revealed a mixed spatial profile of clinic locations. No single variable appeared to define the spatial pattern of clinics. Rather, Anglo proportions (a combination of two racial and ethnic demographic definitions) corresponded most closely with all clinic buffers (Figures 14-16). As in Utah there were cases of significant overlap between variables.

Donor Areas Types

An initial review of the national results provides a rough sketch of donor areas as poorer and more racially and ethnically diverse. However, the state level analysis reflects additional complexity. Relative economic desperation seems to be a constant factor guiding clinic location, but the spatial patterns within the respective states reflects locating practices that are not entirely uniform.

Based upon the analysis there appears to be three types of areas firms are interested in targeting. The first category of community are areas with permanently disadvantaged populations. This includes low-income areas found in the interior of larger metro areas. In the case of Utah this was the most apparent in Salt Lake, Provo, and Ogden. Relative minority status may also explain the differences between Utah and Texas. Black proportions did not register in the analysis of Utah, similarly Hispanic proportions provided little insight for Texas, in some instances, because the state has much higher proportions than the national average. Thus, there were only a few ethnic cleavages that were structured from hot and cold spots, and even fewer that comported with clinic areas.

The second category are areas with temporarily disadvantaged populations. This specifically includes student populations near universities. It should be noted that these two categories are entangled as large cities with economic inequality not attributable to student

populations are typically home to one or more major universities. It should also be noted that the labels are somewhat of a misnomer. While the populations attending college have brighter prospects in general, the institution creates an area of permeant economic precarity that has become socially accepted.

The final area type is exclusive to Texas. There are 19 Texas clinics (roughly 23% of the state's total) that are unified mainly by clustering low incomes and their proximity to the US/Mexico border. With the exception of El Paso, these clinics line the border and are located in smaller and less densely populated areas relative to interior cities and towns. Some of these areas are home to universities but were found to be cold spots of college enrollment. Anecdotal accounts have reported that Mexican citizens cross to donate plasma. If this is the case, it seems likely that cross border donations would make up a sizable proportion of their donors.

Finally, it is worth noting the parameters determined by the HSA. The analysis assesses input data for variation and the ideal scale of analysis. The scale of analysis can be set prior and should be informed by proper neighborhood definition and research question. If a specific distance cannot be justified *a priori*, HSA scrutinizes variation in the data to determine the proper scale of analysis. All scales were determined by the software and proposed an analysis bandwidth between 6.3 and 6.4 miles. This is similar to the 7-mile buffer described in one company's new donor literature. This suggests corporate siting experts, those determining clinic locations, may utilize the same observational units and similar variables. It seems unlikely that differing units of analysis and variables would yield a similar spatial structure by coincidence, though this would be difficult to prove without corporate admission.

Conclusions

A comprehensive spatial profile of for-profit clinic locations remains elusive, but this is not unexpected given geographers' continued struggle with uncertainty of context (Goodchild

2018). However, this research does suggest a general spatial/economic logic to clinic siting practices. Blood components are essential to modern medicine, and by virtue, form a lucrative market. Market-based approaches and technologies have become the norm in the for-profit section of the plasma economy. The US plays an important role in this growing market as the primary source of raw plasma for manufacturing and export. The for-profit industry has proved to be an efficient and generally safe way to procure plasma. This is not to say that because transfusion risks have been reduced, all epidemiological concerns are addressed. Despite reduction of risk this work may still have implications in the realm of public health. Eisenberg-Guyot et al. (2018) found an association between lower health outcomes and fringe economic activities. They suggest that the financial deregulation contributing to industry's growth in the 1980s corresponded with a decline in financial resources among the working class, leading to increases in material and stress effects of exposure to fringe services. Social epidemiologists have shown the significance of spatial dependence and complex relationships between social inequity, space, and health outcomes and would likely find the location of clinics ecologically informative (Krieger 2009). Because market logic permeates many aspects of life, its elements and consequences go unnoticed. Explanations of, let alone reforms to, market operations must be accompanied by the potentially serious effects on human wellbeing in order to highlight these elements (Ollman 2003).

The study's conclusions can be summarized by two major findings. First, the patterns found here synthesize and support conclusions drawn in related studies, while also advancing new understandings of the spatial logic of market forces in the plasma industry. Others have noted that populations adjacent to for profit clinics tend to be poorer and more racially diverse. By using a critical framework, this analysis directly addresses the concerns that James and Mustard's social

index indicates indirectly. Additionally, this work has shown that Volkow's case studies fit within a larger spatial regime of clinic placement.

Second, these findings demonstrate the deficiency of common conceptualizations of plasma and plasma donors. In the course of this research it became apparent that donor framing was critical to informing ethical debates. The donor's framing is already paradoxical and unstable because it involves compensation, which is antithetical to the notion of a gift or donation. Additionally, the exchange relationship is also unclear, as noted above.

The gift vs commodity framing dichotomy that has occupied policy, industry, and academic discourses falls short in ethical debates for two reasons. First, by focusing on commodification of plasma, the donor is minimized, and potentially abstracts away from the donor's environment and experience. Additionally, focusing on commodified plasma does not seem to reflect industry motivations. Firms do not seem to be searching for plasma per se, rather for willing donors. This suggests the importance of distinguishing between plasma and plasma donors when applying the gift vs commodity framework. Minimizing the donor in attempts to conceptualize plasma as a commodity has likely prevented contributions from geographic perspectives.

On the other hand, the commodity vs gift dichotomy cannot easily be applied to donors either. When applied, a commodity framing of plasma donors highlights an under theorized understanding of the commodity. Most of the literature exploring or critiquing plasma as a commodity fails to take up a substantive theoretical discussion of the commodity form. Even the authors responsible for introducing the gift vs commodity framework (Hagen; and to a lesser extent Titmuss) take an understanding of the commodity as given. As a result, attempting to understand the plasma donor and the processes guiding clinic geography are limited.

Despite the limitations of Marxist approaches, the treatment of the commodity as a complicated classification is both an accurate description of the case at hand, and a useful tool for understanding the failure of previous ethical approaches to commodified plasma and plasma donors. In *Das Kapital*, Marx's entry into his analysis of political economy begins with the commodity. Harvey (2010) notes that Marx beginning his critique with an articulation of commodities is important, as he could have begun with other vital concepts like labor, money, or class struggle. Harvey also notes the decision to begin with the concept of commodity was given much consideration. A lengthy treatment of Marx's approach to commodity is beyond the scope of this paper, and is taken up later. However, the point here is that a more nuanced understanding of the commodity form seems necessary to understand a product as complicated as human plasma. Further, a nuanced understanding is also required to understand plasma clinic locations.

Foregrounding plasma donors reveals the need for nuance and consideration of hybrid interpretation. Donors are not layers of shale or veins of coal – at least to the extent they are less fixed. American residents are more mobile than any other national group. Provided this, it would make little sense to exclusively apply a natural resource/commodity conceptualization to Americans and American plasma. An alternative framing might present donors as agents of labor. This conceptualization is rare within literature even though it is potentially useful in thinking about donors as a class (this framing is discussed further in chapter 2). Still this is incomplete as it has only some of the trappings of a labor process, especially in the US. Compensated plasma donation is not regulated by labor laws, taxed as income, or restricted by visa requirements (see chapter 2).

The inability to draw upon the analogies of natural resources or labor in order to think about plasma and donors, respectively, is reflected in the results of the analysis. The national analysis suggests a general areal demographic profile that is targeted, but the finer scale cases

reveal significant spatial variability with clinic areas being characterized in manifold ways. The variability of spatial patterns across place and scale reflects the importance of structural dynamics in maintaining a steady supply of plasma. The nuanced conceptualization of plasma and donors is thus, in geographic terms, a hybrid classification that includes a commodity life cycle similar to natural resources, along with the human elements of labor. Companies concerned with long term economic viability seem to focus on dependable structural markers of willing bodies. Desperate donors can sometimes move and recently depressed areas may gentrify. As a result, companies do not only target bodies but also *areas* of roughly permanent economic precarity. These areas possess a more permanent character though institutional mechanisms, like historically poor groups and neighborhoods, national borders, or universities. Given the need to balance individual donor and areal characteristics, plasma donor areas can be conceptualized somewhere between the fluidity of labor pools and fixed nature of a natural resources.

CHAPTER II

CREATING DONORS AND DONOR GEOGRAPHIES: BLOOD PLASMA INDUSTRY DISCOURSES

Abstract

This article explores the multiple discourses found in blood plasma industry publications. Specifically, this research identifies the dominant discourses utilized to construct industry representations of plasma donors and corresponding donor geographies. Three discourses are identified, all of which concern ethics, public health, and economic ideology. A geographic discourse is also identified and is argued to be an essential part of understanding donor representation.

Key words: plasma, plasmapheresis, economic geography, ethics, discourse

Introduction

This article explores the multiple grammars found in selected blood plasma industry publications. Specifically, this research identifies the dominant discourses utilized to construct industry representations of plasma donors and corresponding donor geographies. After identifying the dominant discourses, it is illustrated how these two constructions are mutually reinforcing and linked to different facets of neoliberal ideological discourse.

First, a brief history of the plasma industry and affiliate institutions is outlined. Next, a sketch of the ethical debate surrounding clinic geography, and the previous literature is discussed. Then it is demonstrated that industry documents acknowledge the practical significance of geography while simultaneously omitting its connection to ethical debates, the industry's image, and the industry's neoliberal perspective on trade and governance.

After explicating discourse analysis as a methodology for textual examination, the method is applied to a plasma trade publication. This involves identifying the voices of authority in documents and outlining the dominant discourses present. Identified discursive themes are those commonly recognized by other social scientists, like those centering on neoliberal ideology, globalization, governance, and responsibility (Dixon and Hapke 2003; Fairclough et al. 2004; Gilbert 2005; Sin 2017). A geographic discourse that can be understood as a scalar bias is also identified.

It is argued that the geographic discourse is an essential part of donor representation, and that it is a response to criticisms leveled against the industry. Additionally, it is argued that industry leaders recognize geography's impact on industry public image and have constructed spatial images counter to many accounts and empirical data. The industry donor discourse seems to be carefully cultivated toward minimizing the connections between clinic locations and ethical concerns of exploitation, and public health risk. Donor and donor geography are two of a few specific topics considered to be loosely linked together under the broader discursive category of neoliberalism.

Blood Plasma

The transfusion of blood components is a vital part of national health. Most countries obtain whole blood (or separated components) for transfusion from donors on a voluntarily and anonymous basis. Blood supplies derived from 100% voluntary non-remunerated blood donation (VNRD) by 2025 is the goal established by the World Health Organization (Garraud and Tissot 2018).

Whole human blood can be divided into three components: plasma (55% by volume), red blood cells (45% by volume), and white blood cells and platelets (<1% by volume). Plasma appears as a clear, yellowish liquid after all other components are removed. It is 90% water with

the remainder constituted by salts, enzymes, antibodies and proteins, and contributes to clotting, material transport, and immunity. In the United States, raw plasma is categorized as either recovered, or sourced, based upon method of collection. According to FDA compliance policy guidelines, recovered plasma is derived from single units of whole blood, or as a by-product resulting from the preparation of blood components from whole blood collection. Whole blood and plasma collected for transfusion is unlikely to come from paid donors because of FDA labeling guidelines established in the 1970s. There was hesitation to use compensated material because of perceived association with elevated levels of transfusion transmitted infection. This led to the decline of hospitals and transfusion services using of paid blood materials (Farrell 2012; Weinstein 2018).

For-profit industries focus primarily on the collection of plasma from paid donors and is rarely used for transfusion (Weinstein 2018). Raw plasma not intended for transfusion (source plasma) can be manufactured into pharmaceutical goods. Given that no synthetic exists, plasma must first be collected from human donors. Source plasma is collected through an automated process called plasmapheresis. During apheresis the plasma component is separated and collected, and remaining constituents are returned to the donor. In the US, source plasma supplies are maintained almost exclusively by for-profit firms collecting from compensated donors (Farrugia, Penrod, and Bult 2010; Farrell 2012). The legacy of US source plasma and recovered plasma originating from paid and volunteer donors, respectively, has been the case for some time (Krever 1997).

Currently hundreds of for-profit plasma clinics exist in the US, but a majority of plasma collected is not intended for domestic use. The U.S. supplies approximately 70 percent of the world's plasma, but accounts for only 40 percent of global demand (Shaefer and Ochoa 2018). Plasma harvested from compensated donors in the US make up a majority the raw plasma

circulating in a growing international market that was last estimated to be worth over 20 billion dollars.

Criticisms of the industry have been rooted in spatial language and perspectives, often citing the areas where clinics are located. Responses from the industry have been numerous. The purpose of this research is to identify the geographic discourses industry representatives have employed to combat criticism of exploitation that are potentially damaging to the industry's image.

History of the PPTA and The Source

The Plasma Protein Therapeutics Association (PPTA) represents the private sector collectors of source plasma and manufacturers of plasma-derived and recombinant analog therapies. The association boasts that "in two and a half short decades, it has become recognized as a global leader and authoritative voice of the plasma protein therapeutics industry (History - Plasma Protein Therapeutics Association PPTA n.d.)."

The organization that would later become the PPTA was originally formed as the International Plasma Products Industry Association (IPPIA) in 1992. The IPPIA organized a European division in 1994, and a North America division in 1998. In 2000 the division merged, finally forming Plasma Protein Therapeutics Association (PPTA). In 2002, PPTA merged with the American Blood Resources Association (ABRA) which added the source division to represent plasma collectors, along with manufacturers (Bult 2010).

The PPTA members produce roughly 80% of plasma therapies in the US and 60% of those manufactured in Europe (About PPTA - Plasma Protein Therapeutics Association n.d.). The number of US independent collectors has declined in the past twenty years, with many centers since becoming vertically integrated into the operation of manufacturers (Bult 2013). The organization is described as "a dynamic trade association that represents a unique sector of the

biologics and biotechnology industry." The mission of the Plasma Protein Therapeutics Association (PPTA) is "to promote the availability of and access to safe and effective plasma protein therapeutics for all patients in the world." and this is achieved through the following

> Fostering the collection of high-quality plasma from healthy donors; Establishing standards for the manufacturing of life-saving plasma protein therapies at the highest levels of safety and quality; Breaking down artificial barriers on trade and compensated donors that limit patient access to therapy; Supporting government reimbursement practices that reflect the unique nature of plasma protein therapies; Educating all stakeholders about the value of the therapies; and Adhering to the PPTA Code of Ethics.

PPTA also administers standards programs that help ensure the quality and safety of plasma collection and manufacturing and protect both donors and patients.

The analysis focuses on knowledge created and disseminated by the PPTA. *The Source*, a quarterly trade publication of the PPTA, serves as a major resource in these efforts. Issues of the trade publication served as the data for discourse analysis. *The Source* is described as "the global magazine of the plasma protein therapeutics industry." The official website dedicated to it, describes its contents:

> With information on international and domestic policy issues, feature stories on patients and plasma donors, medical innovations and other critical industry information; THE SOURCE magazine has been touted as a must read publication for anyone interested in plasma collection, manufacturing, regulatory issues, science and medicine. THE SOURCE offers an attractive, targeted and cost-effective means of reaching decision makers in the plasma protein industry. THE SOURCE is distributed internationally to the leaders in the plasma protein therapeutics, biopharmaceutical and biotechnology industries, as well as patients, regulators and physicians. THE SOURCE reaches over 4,000 subscribers in 75 countries (Plasma Protein Therapeutics Association - The Source 2019).

Every issue of *The Source* begins with a column titled *In My View*. These opening articles are especially informative. They are written in an op-ed and persuasive style and often take a more critical tone toward particular issues concerning the industry. They also include regular use of

rhetorical questions and analogies, aiming their critiques at particular states and organizations. The columns are always penned by the PPTA President and CEO. Because the position serves as the primary spokesperson of the industry, the content of the columns is arguably less affected by editorial influence. Additionally, the content likely reflects most closely an unfiltered message of the organization. They are featured prominently in later discussions.

Discourse Analysis

Discourse analysis is closely linked to the work of post-structuralist thinker Michele Foucault, who used it to disclose characteristics within a text. Characteristics important to the researcher may include unstated assumptions, absences (of particular ideas, voices, or points of view), contradictions, non sequiturs, and dominant metaphors (Barnes and Christophers 2018). One of the chief difficulties of executing meaningful discourse analysis is the 'messy' and multiple meanings of the term discourse. Discourse can be understood as a formalized way of thinking that can be manifested through language. This work follows the definition provided by Michele Foucault, and the later developments of this definition by Sunderland (2004).

Foucault described discourse in ideological terms as "practices which systematically form the objects of which they speak (Foucault 1972, 49)." In this tradition, discourses are about what is thought, who can speak, and with what authority (Foucault 1995), or they may operate as a social boundary defining what can be said about a specific topic (Knezevic et al. 2014).

Burr (2006) expanded Foucault's definition, describing discourse as a collection of meanings, metaphors, representations, images, and narratives that fit together to construct a particular version of the world. Sunderland (2004) has developed Foucault's approach by demonstrating the importance of identifying and naming specific discourses. Sunderland's interpretation of the Foucauldian tradition suggest that discourses are not articulated explicitly, rather traces can be found by looking closely at language and its context. Sunderland (2004)

suggests that anyone who recognizes ‘where a writer/speaker is coming from’, with or without a ‘close reading’ (or ‘listening’), may be said to have provisionally identified a discourse.

Analyzing discourse involves a close reading of a text. The term ‘text’ includes a wide range of media including newspapers, television programs, blogs, architecture, fashion, and furniture (Lockyer 2008). Further, the analysis potentially includes identifying discourses, comparing discourses, and outlining future discursive shifts (Bourke and Lane 2018)

A closely related methodology is textual analysis. Lockyer (2008) describes textual analysis as a method involving examination of either the content and meaning of texts, or their structure and discourse. Texts are deconstructed in order to show the potentially numerous (and often conflicting) meanings or interpretations. Deconstruction allows examination of how a text operates, the manner in which it is constructed, the ways its meanings are produced, and the nature of its meanings (Lockyer 2008; Baker and Ellece 2011). The two methods (text and discourse analysis) demonstrate significant overlap, so much they are presented together in a single entry in the *Handbook of Qualitative Geography Methods* (Dittmer 2009). Baker and Ellece (2011) note that terms textual analysis and discourse analysis have been used interchangeably. Dittmer (2009) also describes engagement with a text itself (including its rhetorical stance, claims to authority, and organization) as a touchstone of discourse analysis.

‘Discourse’ has managed an established status in social theory and research, with much contemporary social research including some form of discourse analysis (Fairclough et al. 2004). But despite its acceptance by many, and its power as an analytical tool, discourse analysis still conjures suspicion from some social scientists. It is often perceived of as too vague and ill-defined, an accusation supported by the numerous definitions of discourse (Fairclough et al. 2004). Similarly, the validity of textual analysis has been questioned. Critics argue that a reading

of a text echoes the perspective of the researcher, leading to an analysis that is as ideological as the object of study.

Like any research methodology, a discourse and textual analytic approach can be more or less valid (Gee 2010). It is important to understand that language is complex and requires close and detailed engagement if it is to be properly and fairly critiqued (Lockyer 2008). It is also important to note that textual analysis presumes texts have their own narrative structures and persuasive qualities, reflecting a design to convey a certain meaning. Analysis does not attempt to identify the 'correct' interpretation, as language and texts are complex and polysemic. However, the instability of language and meaning does not leave interpretations of text infinitely open either. Some interpretations are more possible and likely than others, and it is the role of analysis to draw out such interpretations.

It is important to note that most texts are not pure reflections than can be neatly confined to a single discourse. Within a text, several discourses may be identifiable, and some may be more dominant (readily apparent with the greater proportion of linguistic traces) and some more ephemeral (marginal with fewer, more obscure and tendentious traces). However, being within the same text, it is likely they are semantically and grammatically related.

Together discourse and textual analysis have become a significant methodology in the social sciences, and have been used fruitfully to study economic geography, transformations within geographical education, and public policy (Sin 2017; Barnes and Christophers 2018; Bourke and Lane 2018).

The rigor of the analysis is heavily contingent upon the direct instrumentality of texts under scrutiny. The connection between research aims and selected text should be clearly demonstrated (Dittmer 2009). A great deal of the legitimacy of research conducted with this methodology comes from the research design (i.e., choice of texts, sampling procedures, etc.), as

it is expected that there will be some changes mid-stream regarding the way in which the research is actually conducted. Some texts may prove more fruitful than others, thus leading what had been a 'random' sample of appropriate texts into new 'less random' directions in search of relevant data.

The dataset used in this research spans the Spring 2007 and Spring 2019 issues of *The Source*. The dataset's instrumentality is reflected by the fact that it is the most comprehensive texts of its kind, and by the fact it demonstrates a roughly cohesive voice from the for-profit plasma industry's leading representatives. A typical issue might include any of the following:

- Biopics or interviews of medical professionals, government officials, and representatives of other stakeholder groups.
- Updates on the PPTA's recent activities and initiatives, including lobbying campaigns, organizing events, outreach efforts.
- Summaries of recent industry events and their agendas. This includes conferences, symposiums, workshops, or meetings with regulatory bodies and officials.
- Opinion pieces, one of which is always presented first and authored by the president of the PPTA - the column is titled *in my view*.
- Advertisements for industry products.
- Industry news (e.g., changes to regulations EU or US regulations, ongoing litigation).
- Upcoming industry events.

The data were scrutinized and annotated. *The Source* qualifies its content at the beginning of each issue, stating that because of its interest in encouraging discussions relating to plasma protein therapies, collection, and fractionation, the magazine may contain statements of opinion. Further, it is noted that such statements are those of the author and do not necessarily reflect the

opinion of PPTA or its members. Despite these qualifications there is evidence of editorial authority/guidance. The most compelling evidence of such authority is the discursive coherence in the document reflected by reoccurring themes, talking points, grammar and vocabulary - even many of the interview responses appear contrived given the regular appearance of certain phrases.

Academic critiques of neoliberalism, and all of its injustices, is well trod (Springer 2019). Indeed, neoliberal policy and ideology has damning consequences, but the current trajectory of academic critiques of neoliberalism have plateaued in their utility (Bell and Green 2016; Rowe et al. 2018). The execution of the paper's analysis was attempt with a reflexive and arguably sympathetic reading of the industry documents, working with a certain level of restraint. This balancing reflects division within critical discourse studies (Fairclough et al 2006). Within the field some researchers see discourse analysis as including detailed analysis of samples of actually occurring text and talk, while others do not consider it essential. Fairclough et al (2006) formulates the divisive issue as a question: "is it reasonable to claim to be doing discourse analysis without analyzing actual text or talk in at least moderate detail?" This analysis incorporates a detailed engagement with the literal text – this allows the text to speak with actual examples. But also, at times, go beyond the text to explore latent meanings that emerge when contextualizing the text's content. Processes like omissions of certain perspectives would produce such latent discourses. And additional example of how analysis may go beyond the text is through the multiple functions of discourse. Different discourses can be understood as different perspectives on the world, and a given perspective includes those inhabiting the world and their relations between one another. Thus, in one sense a particular discourse is descriptive. However, discourses can be more than a description of the world as it is (or as it is seen to be), they can also be projective and normative, representing possible worlds that differ from the actual state of affairs.

Representation and Social Construction

The concepts of social construction and representation are pertinent to the application of discourse analysis. Representation involves signifying practices and symbolic systems, and is generally defined as the creation of a mental image through meaning producing practices such as art or language (Hall 1997; Baker and Ellece 2011). Sometimes the term is used interchangeably or in close relations to social construction. Discourse analysis has served as a method for understanding processes of social construction (Dixon and Hapke 2003; Nourpanah and Martin 2016). Discourse analysis is useful in examining how particular phenomena (people, concepts, events etc.) are socially constructed through representative language (Searle 1997; Nourpanah and Martin 2016). Explorations into such connections include an analyses of agricultural legislation, educational initiatives, public health policy, and national identity (Sharp 1993; Dixon and Hapke 2003; Nourpanah and Martin 2016; Bourke and Lane 2018).

The work of Dixon and Hapke (2003) and Sharp (1993) are two relevant examples of how discourse analysis can be used to understand social construction. Dixon and Hapke's (2003) work focused on US agricultural legislation, tracing the emergence and development of an American agrarian discourse, and demonstrated the importance of certain historical sites, institutions, and groups toward knowledge production. Sharp's (1993) seminal work is a classic in the critical geopolitics tradition and made use of discourse analysis in a study of popular conceptions of geopolitics in America through the popular magazine The Reader's Digest from 1980–1990. Aspects of both works are drawn upon here.

Dixon and Hapke (2003) is informative because of its use of discourse analysis in the field of geography, and their development of the concept of "spatialized constructs." They describe a geography of discourse, "which consists of the production, dissemination and consumption of ideas, concepts, theories, and understandings." Their work focused on discursive

sites of production like research centers, media organizations, policy institutes that worked to formulate and disseminate knowledge pertaining to agricultural legislation. More pertinent still is Dixon and Hapke's, "semantic geography." Whereas the geography of discourse describes the physical sites used to produced and legitimize a view of the world, semantic geography is used to understand relationships between ideas in a conceptual space and how certain physical spaces are framed. This framing considers to be a discursively produced geography - one that is imaginative and constructed to achieve certain ends. An example from Dixon and Hapke is the term 'rurality,' which had been mobilized by multiple groups for various ends.

Similar to Sharp (1993), the focus here is on one organization and its flagship publication, the PPTA and *The Source*. Thus, it differs from Dixon and Hapke in that the focus of the analysis is on a particular institutional site and its main publication outlet, rather than locating all sites of knowledge production. The organizational focus is also narrower because of the singular importance of the PPTA and the power it has consolidated since it first emerged. Additionally, here, the focus is on the way donors and donor geography are constructed - by exploring how places and people are discussed (or not discussed) in the text. The suggestion is that a 'talk' about a particular place can aid in creating a geographic 'picture' that is produced as fact. This aspect of the research is similar to Dixon and Hapke's inquiry, especially their second dimension, semantic geography. Semantic geography of discourse refers to the language used to create representations of people and places. Specifically, this analysis scrutinizes the donor and donor geography, and the tension arising from their placement in discussions of product safety and ethics.

Discussion

The data yielded multiple discourses. As previously noted, it is impossible to discretely describe all possible discourses because of the inherent complexity of language, and because of

the interlocking and overlapping nature of many identifiable discourses. Drawing upon Sunderland (2004), who provides guidance in naming and grouping discourses, aids to handle these concerns.

First, Sunderland developed a form of discourse analysis simply referred to as "discourse naming (Sunderland 2004; Baker and Ellece 2011)." Identifying and naming involves a close reading of texts in order to identify linguistic traces suggestive of particular ways of looking at the world or discourses. Sunderland (2004, 28) suggest that

> [P]eople do not . . . recognise a discourse . . . in any straightforward way . . . Not only is it not identified or named, and is not self-evident or visible as a discrete chunk of a given text, it can never be "there" in its entirety. What is there are certain linguistic features: "marks on a page", words spoken or even people's memories of previous conversations . . . which – if sufficient and coherent – may suggest that they are "traces" of a particular discourse.

Linguistic traces can be identified through traditional techniques of discourse analysis (including identifying how social actors are represented, and repetition and co-location of words and phrases). Sunderland's approach also involves identifying how discourses relate to each other. Generally, the relationship between them can be conceived as competing, dominant, mutually supporting, or alternative. Identifying, naming, and relating discourses is closely connected to the project of ordering discourses. Sunderland describes a discourse which subsumes several other discourses under it, as overarching. She suggests it is possible to see networked discourses as constituting an 'order of discourse.' An overarching and dominant discourse usually enjoys 'common sense' status. Drawing upon Sunderland, Baker and Ellece (2011, 84) provide an example dealing with framings of gender:

> A discourse which subsumes several other discourses under it. For example, 'woman as domestic' discourse can be regarded as an overarching discourse under which are more specific discourses such as 'woman as cook', 'woman as nurturer', 'woman as cleaner'. .

> . .The ‘woman as domestic’ discourse itself can also be subsumed under higher order discourses such as ‘gender differences’ or ‘patriarchal society’.

Recognizing that many others could be chosen, identified and explored are three specific discourses (or reoccurring “conversations”) within the text: Positive Image Discourse, Individual Donor(s) Discourse, and Donor Geography Discourse. In the following sections a description of each discourse and the textual evidence supporting the analysis and categorization are given. Ending each section with a brief explanation of how it networks with the subsequent discourses.

Positive Image Discourse

The *positive image discourse* was manifested in two ways. First, the text referenced overt attempts by the industry to rehabilitate and cultivate its image. Second, raw plasma and its products are framed in a way that establishes plasma as lifesaving and uniquely different from pharmaceuticals.

The image discourse is demonstrated by repetition and repeated collocation of words in describing plasma and the omission of widely accepted names for plasma products. The importance and vitalness of plasma is repeated regularly. In literary texts repetition can be used to achieve an aesthetic goal. Repeated phases and structures can also reflect efforts to reintegrate a discourse, making it more prominent significant (Baker and Ellece 2011).

The insistence of plasma’s importance and future potential, is one of the most predominant parts of the image discourse, and is present throughout the entire dataset. Plasma and products are treated as special, and unique. The framing of plasma as unique, and by extension the industry, is also linked to a discourse of scientific authority and is discussed later.

The text draws heavily on regular positive and superlative adjectives within noun phrases. In at least sixteen instances plasma or its derivatives are described as “precious” (for a specific example see Penrod 2007, 26). In another, the plasma derived therapies are described as

"life sustaining." In yet another it's described as "an amazing substance!" This is interpretively identifiable as a marketing discourse, closely affiliated with consumerism, though the 'value' of plasma is consistently linked backed to consumer/patients, rather than profit. This may be to prevent an overly commodified view of plasma, which has historically been negative in the public's eyes.

An example of the positive image discourse is demonstrated in distancing of products from the pharmaceutical industry. A few of the industry's most dominant firms include Grifols, CSL, Octapharma and Shire (which recently acquired Baxter). Grifols, CSL, and Octapharma depend on plasma products for a substantial portion of their revenues, while Shire enjoys a more diversified biomedical based portfolio. Together these companies collect over 80% of the total U.S. source plasma for fractionation. The major companies' global market shares vary between 17%-34% (2018 Grifols investor analyst meeting). This is based upon market shares of IVIG and PIDD therapies. The IVIG market is a well-suited proxy because it generates the highest revenues among all the plasma products. The precise market shares are difficult to ascertain because some of the largest companies are privately owned, in addition to continuous mergers, acquisition, and divisional spinoffs.

However, all of the companies mentioned have substantial interests in the pharmaceuticals market. Yet, despite a majority of plasma used to produce medical therapies, there is little talk of the pharmaceutical industry. Additionally, the pharmaceutical products featured in the text (often referred to by their specific name e.g., albumin, IVIG, etc.) are rarely referred to as pharmaceuticals or drugs. The authors of the text seem to avoid referring to the plasma derived products as drugs or pharmaceuticals. In nearly every instance the products are referred to as therapies, and sometime treatments. This may reflect a rewording strategy attempting to challenge negative connotations, much like a euphemism (Baker and Ellece 2011).

On occasions when there are references to plasma products as drugs or pharmaceuticals the antecedent adjective 'life-saving,' or some derivation of, typically accompanies it. The phrase 'life saving' is found nearly three hundred times in the dataset.

This is potentially a deliberate attempt to minimize profit motives that drive the pharmaceutical industry. The rise of a 'Big Pharma' discourse, which includes both substantive industry criticisms (Iheanacho 2006; Law 2006; Goldacre 2013) and conspiracy theories (Schaffer 2006; Blaskiewicz 2013), is powerful and spans the political spectrum. In a piece aimed at surveying the industry's safety record Farrugia et al (2009, 14) uses the term:

> The products of the plasma protein therapeutics industry have a safety profile which exceeds that of most of the therapies of the other biological sectors and of the products of big pharma. This enviable position is the result of a commitment to product improvements and a state of constant vigilance . . ..

There are other attempts to distinguish the industry, and distance it from, the negative image of big pharma. These efforts are an important marker for identifying discourse. As Sharp (1993) has noted, discourses often work toward, and are centered on, structuring difference. In an article critical of how European governments and the EU have used taxpayer resources, PPTA President Bult closes by simultaneously taking the moral high ground and distinguishing his industry from the broader pharmaceutical industry

> I will stay away from the political debate and instead focus on helping patients in different parts of the world to have unlimited access to lifesaving plasma protein therapies. The costs for the therapies we deal with only represent 2 percent of the total costs for medication used in the world. The therapies are truly different than the traditional therapeutics made by Big Pharma. Though we are small in comparison, the enormous contribution made to the recipients of plasma protein therapies is the chance for a normal life. Taxpayer money could be much better spent to provide good care to patients, especially those with life-threatening, genetic conditions.

Von Hoegen (2011, 9) writes similarly in a piece discussing European regulatory frameworks. The multiple parts of the positive image discourse are included (noting its special status, uniqueness, lifesaving capabilities, and distinction from 'big pharma')

> A glance at PPTA correspondance or promotional materials reveals the focus of this Association and the medicinal products produced by its members: biological lifesaving therapies either recombinant or fractionated from a very unique starting material—human plasma. In essence, what PPTA represents is not "Big Pharma," but a very specific niche sector serving patients with rare diseases. To further highlight their uniqueness these plasma protein therapies are exempted from biological products regulations from the European Medicines Agency (EMA) and World Health Organisation (WHO) biosimilars guidelines.

The image discourse is more explicitly demonstrated by the text's account of its parent organization's institutional developments dedicated to improving industry image. One piece appearing early in the data set titled *Industry Image Top of Mind for Source Plasma Collectors* (Kilbourne 2008) was dedicated entirely to the topic. This marked the beginning of a consolidated effort dedicated to the industry's image. Kilbourne (2008, 8) writes

> It's a challenge to get our point of view across in media stories regarding plasma collection and the coverage the industry has seen lately is really an economic story rather than a story about plasma donation and life-saving therapies. Some media stories are more balanced than others and this underscores the need to engage with reporters to provide information about our industry and provide context for stories on plasma collection.

In response to these challenges from media inquiries, the PPTA developed and disseminated a "tool kit of resources" that included "suggested media talking points that provided appropriate industry messages regarding plasma donation (Kilbourne 2008)" This initiative reflected a strategic imperative among association members to be "consistent when it comes to information regarding the industry as a whole." There would eventually be an institutional response from the PPTA. In reporting on the PPTA's activities, The Source highlighted a new effort at building the

industry's image and the formation of a new group was announced. The Source Image Task Force, along with other groups would develop The Source Industry Image and Credibility Campaign (Inside PPTA 2009, 30). The campaign was designed to profile the source plasma collection industry to the general public. In describing the tactics used Penrod (2011, 16) writes:

> These and other efforts have also resulted in increases in intangible benefits as well, such as an enhanced ability to distribute key messages to personnel in member companies responding to media inquiries. As a result of these new capabilities, negative media impact and misperceptions about the industry have been minimized and, in some cases, turned to positive messages about the importance of plasma.

The campaign was part of a broader strategic plan to rehabilitate a previously damaged image through an "effort to bring coherent messages about [the] industry to as many diverse audiences as possible (Penrod 2011, 16)." The discourses surrounding industry image demonstrate are linked to the other two discourses covered - donor discourse and donor geography discourse. The image campaign regularly references safety, quality, access, and ethics, and these themes reemerge in discussions of donor health and donor geography. This connection is also evidenced by the organizing of International Plasma Awareness Week (IPAW). This discursive connection has two dimensions. First, the IPAW was first organized by the Source Image Profile Committee - its predecessor group, the Industry Image Task Force (The Imperative for an International Awareness Event 2013). Second, discourse surrounding IPAW graphs the language of plasma products unique nature, lifesaving potential, and vital importance on to donors and donations. The stated goals of IPAW are:

1. to raise global awareness about source plasma collection.
2. recognize the contributions of plasma donors to saving and improving lives.
3. increase understanding about lifesaving plasma protein therapies and rare diseases.

The introductory article (The Imperative for an International Awareness Event 2013) of the inaugural IPAW connects the manifold components of the positive image discourse – plasma's unique and essential nature, lifesaving capabilities, and altruistic source (donors):

> Plasma does not grow on trees; the global demand for plasma protein therapies continues to increase. Every day *thousands of people around the world make a conscious and voluntary decision to donate plasma for others who depend on the lifesaving therapies* manufactured from it. Despite its *vital importance* for so many patients, *plasma donation* by plasmapheresis is virtually unknown to many, which limits the potential of finding new plasma donors. International Plasma Awareness Week (IPAW) is one way to spread the word and let more people around the globe know about the *importance of donating plasma* (emphasis added).

The article continues similarly

> Those fortunate enough to work in this industry are already aware of how plasma protein therapies save and improve lives, now we get to show our appreciation to those who deserve much respect and make it all possible—our plasma donors.

The positive image discourse is expectedly the most apparent, often operating similarly to discourses found in a typical advertising or marketing campaign. However, it may also be the most multifaceted. The previous discussion argues the relation and intertextuality between industry image, donors, and donor geography (and is discussed further later). Additionally, the positive image discourse seems to be part of broader efforts to convince the public, and policy makers, of the unique nature and vital importance of plasma products *and* the industry itself – this generally includes its many actors, institutions, and practices. Stated differently, plasma's uniqueness is drawn upon as part of a science/authority discourse. This equates a framing of the industry as a benevolent scientific authority that is not likely to have conflicting interests associated with profit generation. The impetus for credibility and positive image building efforts is omitted. The most likely reason for industry distrust is the historical examples of industry

negligence, in particular instances where patient consumers were knowingly exposed to infectious diseases.

The following excerpts are from a single article dedicated to the industry's safety record. Farrugia et al (2009, 8), notes once again how unique the industry is:

> This industry is very different from traditional pharmaceuticals. Manufacturing plasma protein therapies that are infused or injected by patients results in the formulation of a unique class of biologics that are dissimilar from chemical compounds. PPTA member companies exemplify vigilance and innovation through the various safety measures that have been implemented over the decades. . ..

This difference is reiterated (referencing 'big pharma') and tied to safety protocols

> The products of the plasma protein therapeutics industry have a safety profile which exceeds that of most of the therapies of the other biological sectors and of the products of big pharma. This enviable position is the result of a commitment to product improvements and a state of constant vigilance to ensure currency in safety, quality and efficacy.

The industry and its activities are distanced from 'big pharma,' a segment of the economy that has recently been demonized in the wake of the US opioid epidemic for maximizing profit to the detriment of patient safety and scientific rigor. The author takes care to mention voluntary industry reforms that were ahead of government mandates (this is noted repeatedly throughout the dataset). These reforms occurred in the wake of the 1980s HIV epidemic. This suggests that the industry was, and continues to be, ahead of government regulatory efforts. It is worth noting the documented instances in which industry officials ignored suggested safety measures and early warnings from public bodies like the CDC. This ultimately led to companies knowingly exposing patients to untreated plasma (Starr 1998; Garner 2018).

In highlighting a particular industry working group the authors (Farrugia, Gustafson, and von Hoegen 2009, 16) build the credibility of the for-profit industry:

> In 1994 the Virus Safety Working Group (VSWG (Later Pathogen Safety Steering Committee or PSSC) was established as the industry's scientific expert committee to address virus safety issues of plasma protein therapies on a global basis. *The members of this PPTA expert group on pathogen safety are all well-seasoned scientists striving to remain accepted members within the scientific community, while at the same time ensuring that within their commercial environment pathogen safety of plasma protein therapies is always addressed according to state-of-the-art developments in technology.. . ..*Over the years since its foundation the PSSC has established itself as the globally accepted industry expert group on issues related to the safety of plasma protein therapies. . . .The experts monitor, assess and comment on newly emerging pathogens and are responsible for advancing the scientific credibility of the industry (emphasis added).

In the same article the author highlights the fact the PSSC is recognized and has work alongside regulatory agencies in both the US and Europe and the WHO.

Taken alone these excerpts are not unusual. More interesting is the presence of anti-regulatory traces found in the text. Together the efforts to build private business credibility while critiquing public institution are hallmarks of neoliberalism. In a piece title "To Build or Not to Build?" Waller (2007) encourages governments to reflect on decisions to build plasma manufacturing plants. Specifically, he covers cost effectiveness, ethics, patient interest, self-sufficiency and guidance. The article explores whether it is more beneficial to continue dependence on imported plasma proteins produced and supplied by international market mechanisms, or to aspire for national self-sufficiency, by manufacturing nationally derived plasma in a national facility. The debate is immediately framed in terms of tension between bureaucrats motivated by electoral politics and nationalism, and industry. Nationalism is also invoked as an obstacle to the liberal global marketplace:

> To a politician, the answer to this question seems like "a no brainer" – it's obvious. Even if it costs a lot, even if our country will have to go on financially supporting the facility for a long time into the future we just can't trust foreigners help us meet our fellow citizens' needs. The enormous costs can be defended on the basis of old fashioned nationalism – always a popular cause with politicians. It is curious then that plasma proteins are the only pharmaceuticals where politicians and ministries of health have this debate. There is very little debate

> regarding the dependence on “foreigners” to meet the demand for vaccines or other medicines in the contemporary doctor’s “tool kit”.

National regulators serve as a foil to characterize the industry as the authority on scientific and regulatory matters. However, this discourse can be mobilized to subtly to undermine public institutions. Waller (2007) continues, presenting the closure of national fractionation plants as related to competency:

> Despite the fact that the money was all spent, neither facility will ever produce a gram or an international unit of anything. The details are irrelevant here, but these real cases demonstrate the need for tight controls and the importance of getting sound advice from *skilled, competent professionals and not just by those who stand to gain from the project going ahead* (emphasis added).

Again, there is an adversarial framing, with not only motivations of public servants being questioned but also their competency. Waller contends that avoiding commercial dependence is financially unsustainable and irresponsible. The discussion culminates in advocacy for a free market approaches in which governments contract with commercial plasma manufacturers (Waller, 2007, 21):

> The best route of ensuring a sustainable supply of plasma derivatives at the best prices is to engage in normal contracting that is as close to the end user . . . as possible. Health authorities that contract in this way can be confident that what they have ordered will be delivered. If the inbuilt challenges of producing biological medicines cause a disruption in supply then it is the responsibility of the manufacturer to find an acceptable alternative and to bear the cost of any difference in price. If governments or health services, like the majority, choose not to build a fractionation plant but nonetheless want to meet the clinical needs of their fellow citizens from nationally collected blood or plasma then what are the options. The first question relates to the quality of the plasma to be fractionated. If it meets the high standards required by regulators in most developed countries then they can consider “contract fractionation” and come to an agreement with a competent manufacturer.

Perhaps most interesting is that this same discourse was evident in the lead up to the HIV epidemic. Industry representatives described early warnings as evidentially weak, or

ideologically/politically motivated (Starr 1998). An important perspective eschewed here is that public servants must consider public goods of policy decisions, a variable with which private industry is not encumbered.

Another example of the science/authority discourse appears in the context of industry safety. In a piece titled "Decades of Safety Measures," Farrugia et al (2009, 8) describes the safety measures the plasma protein therapeutics industry has put in place over the years to demonstrate its commitment to safety. The authors then parlay the credentials into a critique of industry regulators

> PSSC has had many achievements and successes over the years of which the introduction of industry wide standards for HIV, Hepatitis B virus (HBV), Hepatitis C virus (HCV) and Parvovirus B19 have to be regarded as the most significant initiatives to raise the credibility of the industry and assuring patients, physicians and regulators about the margin of safety of these often life-saving medicines. *The Parvovirus B19 standard can serve as an example of how a proactive industry initiative can assure stakeholders and at the same time hold up unnecessary regulatory constraints.* The Parvovirus B19 standard was introduced in 2000 in reaction to concern about its impact to the patient community, particularly to pregnant women. The standard set a cut-off limit for Parvovirus B19 in the plasma pool of 105 IU/ml and has proven its value since its introduction, by simultaneously avoiding unnecessary loss of the precious starting material, human plasma. *It is very unfortunate that despite the abundance of available experience over the years U.S. regulators have recently decided to require a cut-off limit of 104 IU/ml.* European regulators have refrained from considering a similar approach in the context of the revision of the Note for Guidance on plasma-derived medicinal products (emphasis added) (see also von Hoegen 2009)

A final related component of the science/authority discourse is industry's willingness to question scientifically accepted standards of measuring medical efficacy. The industry wants to command the authority of science for the private sector while simultaneously undermining its use by the public sector. This is often situated alongside a conflicting free market discourse. There are two examples of the science authority discourse and its tensions with free market logic.

First, there are repeated critiques of using medical science to scrutinize plasma derived therapies, in particular albumin. Albumin, one of the more lucrative derived plasma products, has

the longest history of use. In a piece title "Albumin: History and Controversy" Farrugia (2008) demonstrates industry frustration with scientific scrutiny. Many practices and institutions are formed and reaffirmed without the support of empirical testing. In the case of scrutinizing albumin, the PPTA is critical of scientific standards, preferring instead that product safety and affinity rest upon temporally, but not empirically rigorous, support. Farrugia justifies the PPTA's concern regarding guidelines for blood components and plasma derivatives produced by the German Medical Association (Bundesärztekammer), which he suggests throws "doubts on the safety and efficacy of albumin, which are unreflective of modern knowledge of this important therapy." Farrugia justifies his concerns

> . . . it is the case that albumin, like many medicines that have been established in medical practice for many years, *has not been subjected to the same level of investigation that current drugs have to undergo before they are approved for the market*. It is difficult to carry out clinical trials in areas of established practice, and such trials are very expensive. With a relatively established and "unglamorous" drug like albumin, the demands of modern day Evidence-based medicine (EBM) are very onerous and not always possible to satisfy. This has led to continuing pressure to demonstrate the safety and efficacy of albumin relative to other therapies (emphasis added).

The topic is visited again by Farrugia (Farrugia 2010, 2012a) in pieces titled "Reflections on the Use of Albumin in Clinical Medicine: Tradition or Therapeutic?" and "History of Plasma Protein Therapies: The Era of Fulfillment (1992–2012)." Farrugia is critical of "advocates of evidence-based medicine" and their concern of the relative safety of albumin and the need to 'prove' its safety and efficacy through clinical trials. He cites a major 2004 Saline versus Albumin Fluid Evaluation (SAFE) trial study to dispel doubts related to a 1998 meta-analysis:

> Indeed, in a meta-analysis1 claiming to summarize such trials, the prestigious Cochrane Collaboration claimed in 1998 that albumin was unsafe. This led to a lot of doubts on the future of the product. Large randomized clinical trial carried out in Australasia—the so-called SAFE trial study—which showed that albumin given to patients in intensive care was truly safe.

However, the SAFE study only concluded that ICU patients use of either 4 percent albumin or normal saline for fluid resuscitation resulted in similar outcomes. While the study was well received, some voiced major concerns over misconceptions that would arise by relying too heavily on a single clinical trial, and ignoring conflicting results from patients subsets (Cook 2004; Haynes and Berman 2004). Adherence to the rigors of establish scientific methods appears to be readily jettisoned when used to scrutinize efficacy of plasma products. Certainly, patient demographics related to orphan diseases demands flexibility, as the rigors of clinical trials are difficult to apply to orphan disease. However, methodical advances have made small population clinical trials more accessible and reliable (Day et al. 2018; Friede et al. 2018).

Additionally, issues of small population size do not explain the PPTA's criticism and/or skepticism of Comparative Effectiveness Research (CER). Cost-effectiveness analysis, a form of health technology assessment, is a government and regulatory method for assessing the gains in health relative to costs of different interventions. It is important to note that it is only one of many criteria used to allocate resources, though it is considered vital because it directly relates the financial and scientific implications of different interventions (Jamison et al. 2006). The Source included multiple pieces critical of Comparative Effectiveness Research. The PPTA's official stance suggest its primarily objection is not to CER *per se*, but only any meaningful use of its research toward policy:

> The PPTA is not oppose to such research but will continue its efforts in advocating for comparative effectiveness research that does not proscribe government-based coverage determinations through restrictive formularies that would negatively affect patient access to life-saving plasma protein therapies.

One of Farrugia's (2014) chief critiques of CER is that work of regulatory agencies should be detached from issues pertaining to costs and reimbursement. Further, he suggests approval to enter the market should be based solely on evidence of safety, quality and efficacy.

Thus, the question as to whether a therapy is safe and efficacious is separate from cost (see also Farrugia et al. 2015). He writes that “If regulators had to include cost issues in their review, the primacy of safety and efficacy might be undermined.” This seems to create tension between conflicting discourses as profit motives encourage by market mechanism have also undermined the primacy of safety and efficacy.

Interestingly CER is likely more flexible than a strict adherence to clinical trials. It generally does not include placebo-controlled trials and often focuses on broader, more heterogeneous populations (i.e., "real world" populations). CER is the generation knowledge and synthesis of evidence comparing the benefits and harms of alternative methods to prevent, diagnose, treat and monitor a clinical condition, or to improve the delivery of care. The goal is to provide stakeholders (patients, providers, payers, policy makers, etc.) with information to make decisions about the benefits/cost between two or more tests, treatments, interventions, delivery systems, or policies. The purpose of CER, as stated by the Institute of Medicine in its 2009 report on Initial National Priorities for Comparative Effectiveness Research, is to assist consumers, clinicians, purchasers and policy makers in making informed decisions that will improve health care at both the individual and population levels. Evidence is generated through a variety of study designs including observational and clinical trials (among other design types) and represents synthesis produced through systematic review.

This may seem counter intuitive but, it is interpretable through a political economy lens. A possible grand thesis unifying these observations relates the current legitimacy crises and neoliberalism. The increasing lack of trust in public experts and regulatory officials is potentially related to decades of neoliberal policy in the developed world. This theory is supported by Deneen (2018) and his survey of failures produced by liberal politics. Pertinent is his articulation of liberalism as essentially ideological despite its wide historical presentation as otherwise. The

PPTA is admittedly supportive of market mechanisms in distributing industry products. And, as Deneen has described, the PPTA considers deviation from ostensibly neutral market mechanisms must be the result of ideological meddling. Dismissal of policy beyond a liberal framework as ideology is apparent in debates over the construction of nationalized fractionating plants. It is further evidenced by documented remarks in reporting on a recent PPTA hosted forum. According to Birkofer (2015) during a presentation on the topic of national self-sufficiency Dr. James Stacey Taylor urged stakeholders to demand better evidence when policymakers asserted that self-sufficiency was the best option for countries to meet the needs of their citizens. In her reporting Birkofer quotes Dr. Taylor

> When a country which pursues national self-sufficiency in blood or plasma or any other medical product that it can import cheaper, it's wasting its health care resources on an ideological, ideologically-motivated policy. . . . In human terms, this means that it is not helping its patients in the way that it should. It's spending money badly.

Taylor is a moral philosopher that has argued the application of market mechanisms in distributing human organs is morally imperative. He has also written in defense of universal commodification.

Relating neoliberalism and institutional erosion is usually described as a decline of cultural/religious values. Understanding its erosion of scientific institutions is less clear, because neoliberalism is regularly presented alongside empirically rooted enlightenment values and liberal deliberative democracy – or classical liberalism, its ostensible historical forebearer. One might expect that scientific institutions would be unaffected by a crisis of legitimacy brought about by liberal policy shifts, however, climate and vaccine skepticism suggests otherwise. Similarly, the PPTA seems to contribute to the erosion of national regulatory institutions, and even the World Health Organization.

The selective deployment of scientific authority and allegedly rational/deliberative arguments supportive of industry economic interests, reflects Deneen's understanding of the liberal project as ideology. A combination of discourses used by the industry related to government, science, and the economy could reflect the primacy of capital accumulation in the industry, despite *The Source's* regular appeals to ethics, science, and justice. The debates in question can be characterized by dialectical tensions:

Table 1. Neoliberal Dichotomies

Global market mechanisms	Support for government subsidization of industry products
Limited government involvement in industry/market	Regular lobbying and intervention in government regulatory process
Scientific Authority of supporting product efficacy	Irregular application of scientific standards
Dedication to access	Resistance to biosimilar approvals

Structuring of patient access is a final example of neoliberal framing in service of industry image. Patient access is a major concern for PPTA and its membership. However, the threats to access that are identified in the text are almost exclusively barriers to free trade. Threats to market-based access are typically described as 'barriers' and include policies that relate to trade regulation, safety regulation, or national self-sufficiency. This extends to government reimbursement policies as well. Despite alleged concerns for government spending and efficiency, the PPTA regularly advocates for expanding subsidization of their products. Public subsidization of the private sector is also regularly associated with the neoliberal paradigm (Chomsky 2007). Product pricing and its relationship to the industry's impressive performance in the market over the past 30 years is seemingly never framed as a potential risk to access.

Donor(s) Discourse

The discursive formation of donor and donor geography is complex and nuanced. First, donor and donor status are negatively constructed by the absence of representation as a stakeholder group. There are numerous examples of collaboration between stakeholder groups working toward mutually beneficial goals (for excellent examples see Bult 2014a, 2014b). Examples include lobbying efforts related to reimbursement policy, and advocating for plasma pharmaceuticals addition to the WHO's essential medicines list. Stakeholders regularly include governmental and regulatory officials, collectors and fractionators, patients, and health care providers.

The only donor stakeholder group found within the text was the International Federation of Blood Donor Organization's (IFBDO). The IFBDO submitted a letter to EU regulatory officials advocating for non-remunerated collections of plasma. The PPTA article included a short but scathing rebuttal to the organization's advocacy. The IFBDO is a narrowly focused organization whose stated goals are "to promote the regular, anonymous, voluntary, non-remunerated gift of blood in all countries of the world" and "to combat all forms of marketing and gain with respect to blood and blood derivatives, under the principle that the human body is inalienable."

This exclusion of donors as stakeholders is likely linked to the subtle, but prevalent, discourse of gratitude. The discourse of gratitude aids in understanding why donors are considered the "cornerstone" of the industry, and their gift "a precious starting material," but they do not have regular stakeholder status through a recognized group organization. This seems similar to discourses of gratitude reflected in neoliberal practices. For instance, worker appreciation celebrations may be held to prevent labor organizing or in lieu of offering wage and benefit increases.

There are multiple discussions surrounding donor compensation, the PPTA position's resoundingly supportive of the practice, arguing it is essential to meeting demand and expanding access to plasma products (See Taylor 2014; Bult 2018). The industry's discursive treatment of donors is one of gratitude and appreciation and is evident in a recent PPTA response to Shafer and Ochoa's (2018) piece in *The Atlantic*. The piece explored the ethics of plasma procurement and questioned the extent to which the sellers were 'voluntarily' offered what the industry describes as a 'donation'. Additionally, they noted the potentially reinforcing connection between weakening social safety nets and a growing plasma industry. The PPTA responded promptly with an official statement:

> The article, "How Blood-Plasma Companies Target the Poorest Americans," by H. Luke Shaefer and Analidis Ochoa, published in The Atlantic on March 15, was unfair to plasma donors as well as to individuals living with rare, genetic, and chronic diseases who rely on access to plasma protein therapies. Plasma donors *are due our gratitude and respect*, not sweeping negative characterizations. Regardless of their motivations, these donations save the lives of men, women, and children facing life-threatening diseases. . .. As a trade association, we are prohibited from discussing or interfering in any individual company's business practices. That said, PPTA thanks all plasma donors for their contribution to making life-saving medications for people all over the world. Without their commitment, those living with these diseases would go untreated. On March 13, PPTA launched the global "How Is Your Day?" initiative, whose goals are to differentiate plasma protein therapies from traditional pharmaceuticals and show the value they provide to individuals who rely on access to these unique biologic medicines. As part of the initiative, plasma donors discuss why they are committed to providing their plasma, and patients share their stories and give thanks to donors worldwide

The response is deflective. A critique of the industry extractive practices is framed as a critique of donors and product recipients. That Shafer and Ochoa's class description of the donor base is interpreted as a negative characterization is also telling. This is likely due to the discursive link between industry image and donor mythology. In one interview a PPTA representative reflected on the role of plasma donors and their link to the image of the industry:

> Q: What do you see as the most important task that you will have as PPTA 's Chairman?
>
> A: The reputation of the industry that has been built over the last two decades has created a foundation of quality and safety. This quality starts with the plasma donor. From the start, we focus on donor selection and testing, followed by advanced viral inactivation technologies to protect the patients using our therapies.

Direct references to donor(s) work to construct a representative donor and are most related to a discourse of geography. The direct references reflect two scales. First, there are direct references to donors, collectively, i.e., in their entirety. These coarser scale references are seen in patient biopics, hypothetical speak, and expository pieces aimed at allegedly educating readers about the realities of donors. Newkirk, CSL's Director of Marketing Chairman of the PPTA Source Industry Profile Committee, references all donors collectively when discussing IPAW. He views IPAW as "yet another opportunity to recognize our valued plasma donors and their role in helping to provide therapies for patients with rare and serious diseases." And again

> CSL Plasma is using this week to promote greater understanding and appreciation among patients, employees and donors alike. In particular, during this week CSL Plasma staff will be thanking donors for their time and highlighting the impact their donations have on patients' lives.

The following references are characteristic of how donors are presented and discussed and provides examples of the coarse scale structuring of donors through generalities and hypothetical speak:

> We value plasma donors for their contributions toward saving patients' lives. It is important that industry has this new tool to further ensure that the donor experience goes smoothly and safely.
>
> . . .the world supply of plasma derivatives (and hence the patients who depend on them) is strongly dependent on the U.S. source plasma industry and its compensated donors.
>
> . . .the geographic diversity of the modern donor base.

Patient biopics regularly reference all donors while reflecting patient gratitude and donor necessity. An example biopic titled, “Patient with Primary Immunodeficiency Disease says Thanks! To Plasma Donors for Helping Her get her Life Back,” demonstrates this. The biopic describes the patient’s life before and after her CVID diagnosis and treatment with immune globulin therapy.

> Judy also is quick to thank plasma donors who make it possible for her to lead a healthier, productive life. “With this donation, this gift from people giving plasma – they are doing for me what I can’t do on my own,” she says. “This is a huge gift whether [plasma donors] realize it or not.” Judy says there is no way to describe how she felt before she started her Ig therapy, explaining how she would fall asleep during rock concerts she attended with her teenage daughter. “I was barely functioning as a parent and now I’m a mom again. I owe my life to the donors.”

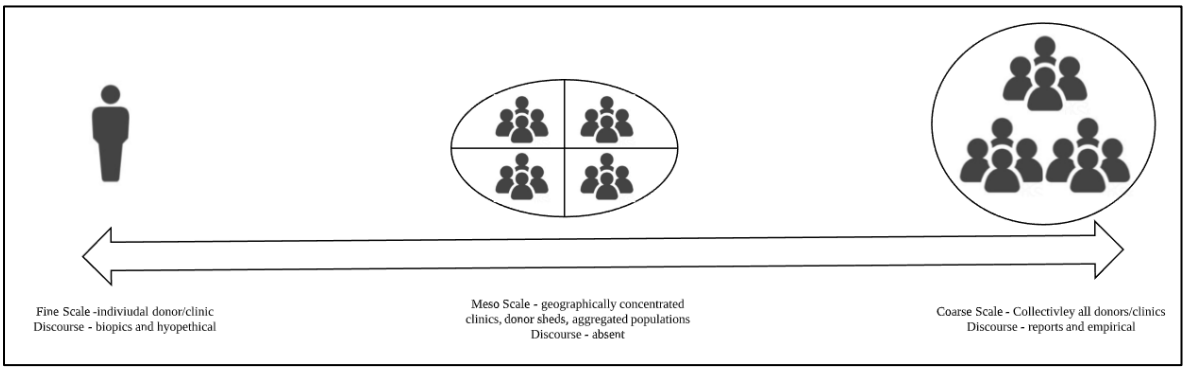
Again, the author links and aligns the story to PPTA policy agenda for getting product subsidized:

> Judy describes health insurance coverage as the biggest and most stressful issue facing families coping with PIDD. “The product is available, but it has to do with reimbursement issues and getting insurance to pay.” Many individuals with chronic illnesses like primary immunodeficiency diseases risk hitting the maximum lifetime benefit of their health insurance. “The problem is that you are backed into a wall and need the medicine to survive or to have any quality of life, and there are no easy solutions out there right now if you don’t get insurance with a high lifetime cap or meet criteria for public assistance,” she says. The situation scares Judy because she will need the therapy forever. “I’m very, very lucky insurance has stood by me – so many people don’t have that”.

Referring to all donors collectively (i.e., the donor base broadly conceived) even in “geographic terms” as seen in the last quote, is not geographic. It is only when the donor base is dis-aggregated and subdivided can the geographic clues of exploitation emerge.

Direct references also appear through publication of intimate biopics on particular donors and their experiences. The scalar distinction between types of direct references (individual donors vs all donors) is important to understanding discourses of donor geography. It is only at the meso scale that clinic geography and donor geography can be brought together (Figure 15).

Figure 15. Scalar Language and Discourse



An example donor biopic can be found in the 2009 Winter issue of *The Source*. The biopic is titled "Ohio Brothers dedicate more than a decade to Giving Plasma" and describes Samuel and Alvin Collier's motivations and experiences donating plasma at a Biotest clinic in the rustbelt town of Youngstown Pennsylvania. The piece, provided to *The Source* by Biotest Pharmaceuticals, states that the brothers donated more than 1,200 units of plasma in a 10-year span. Another example comes from outside the US. The biopic is titled "Plasma Donation —A Family Affair", and highlights the Skrzipczyk family of Nürnberg (Bavaria-Germany) and their experience of plasma donation as a family affair:

> The father, Peter Skrzipczyk (59), made his first plasma donation in 1982. Since then, he has donated more than 1,100 times. Peter, who works for an insurance company, is also very active as an advocate among patients and politicians. For him, it is crucial to educate people about the importance of plasma donation and the lifesaving products that are made from it. His wife, Petra (52), works as an accountant and decided one day in 1995 to go with her husband to the donation center. She enjoyed the atmosphere in the center, especially the friendly staff, and helping others by making a small contribution made her feel good. Since that day, she has donated about 760 times. Seeing his parents acting as lifesavers and convinced by the importance of this cause, their son, Maximillian, waited impatiently for his 18th birthday in 2010 to finally start donating plasma. And he can be proud: To date, the 27-year-old graphic designer has already donated more than 230 times. Altogether, the Skrzipczyk family has donated more than 2,000 times! . . . For the Skrzipczyks, every plasma donation counts in the life of a patient. . . .This year marked the center's 40th anniversary, which was celebrated during IPAW. . . .This is why—in the name of all patients who rely on therapies made out of human plasma—we would like to thank the Skrzipczyks for their incredible commitment. They are true lifesavers!

Another German example title “German Donor Makes Remarkable Contribution” highlights the contributions of Ralf Riedel. The biopic is situated alongside German regulatory changes to plasma donations:

> The German regulatory system only recently increased the annual number of permitted donations from 37 to 45. Given that, the high level of engagement and commitment demonstrated by Ralf Riedel is more than impressive. Mr. Riedel has donated plasma 430 times. . .. With the investment of a few hours per donation for more than 20 years, Ralf Riedel has contributed to improving and to saving a multitude of lives. In his modest way, he has assumed responsibility for a larger cause and to help other people without getting anything in return. Riedel intends to donate for the next 20 years or another 400+ donations.

It is worth noting that all of the individual donor biopics identified in this study did not seem to capture the experience of the average donor. Of the three-examples highlighted here two were, in Germany (see also *The Source* Winter 2008, 20). German donors do not reflect the average donor experience because they supply only a small proportion of raw plasma needed for the global market. Additionally, Germany provides substantially more social welfare measures to its citizenry than the global leader in plasma export, the US, possibly suggesting a link between high plasma exports and a deficient amount of social safety nets. Even when compared in per capita terms the US doubles German output (a phrase rarely uttered) (Farrugia 2012b).

The US example is not representative either, as it included donors participating in a program dedicated to collecting plasma with unique properties (sometimes acquired through special immunizations) – such programs compensated substantially more than the average donation.

Donor Geography Discourses

Donor geography discourse is directly related to the way in which donors are represented and described. Sharp (1993) has demonstrated that while many geographic facts are agreed upon; the use of geographic description is always selective. Further, Marston (2000) has shown that

components of geographic scale are not immune to social constructivist critique. The data suggests that donor geography is constructed by selective, scale conscious descriptions of the donor(s). As demonstrated construction comes by way of personal biopics (fine scale) and reference to all donors and related statistics (course scale). A more complete, and arguably objective, description of donor geography would include data drawn from multiple scales. Meso scale representations are conspicuously missing from the data. This may be a product of the fact that such descriptions would harm the industry's carefully cultivated image and would support long standing critiques related to targeting economically precarious communities.

The conceptual link between the donor and donor geography is illustrated in the few mentions of clinic locations. Interestingly these are the only instances in which clinic location, donor areas, and ethical concerns are mentioned together. The scarcity of direct references to geographically specified donor communities is interesting when considering that plasma donors are the most fundamental component to therapy production. Related, and equally telling, is that the phrase "clinic location" is found only once in the entire data set.

When referenced, donors are referred only individually or collectively. As noted, what appears to be missing is a meso scale donor discourse. An example would be references to donors of a specific neighborhood or even a city. The deliberate nature of this avoidance is evidenced through two examples. First, while a majority of the data has no trace of meso scale descriptions of donor geography, it was unavoidably referred to in the context of epidemiology. It appears specifically in relation to discussion of PPTA safety measures and methodologies.

The data is characterized primarily by an avoidance of discourses centered on geographically specified communities. Despite this some traces are arguably unavoidable because a key feature of epidemiology is the measurement of disease outcomes in relation to a population at risk (Coggon et al 2009). Further, assessing risk requires a population to be geographically

defined. As result there here is a mesoscale articulation in two specific PPTA epidemiological protocols.

Industry representatives and the PPTA understand the epidemiological importance of subsections/segments of a population. This is demonstrated through epidemiological discussions found in the International Quality Plasma Program (IQPP) standards. IQPP standards are voluntary, industry derived, practices aimed at ensuring source plasma is of the highest quality. Centers that receive IQPP certification are routinely audited for compliance with standards. There are seven standards, though two specifically demonstrate the industry's recognition of the importance of donor geography, specifically meso scaled donor communities.

Clinics and geography are rarely co-located in the text, rather they are compartmentalized. Meso scale donor geography is important to the industry because it is the necessary scalar lens for reducing epidemiological risks. For this reason, it forms one of the IQPP standards. The Community-Based Donor standard states

> The ultimate safety of these therapeutics is critically dependent upon the quality of the source material from which they are derived. IQPP-certified plasma centers accept only donors who live within the plasma center's defined *Donor Recruitment Area* (DRA). Donors must provide valid photo identification and proof of a local residence. . .. In addition, donors who reside outside of the defined DRA in which the plasma center is located will not be accepted. Exceptions are made only for area college students, members of a local military installation, or approved donors who possess unique antibodies for special collection programs. The Community-Based Donor Standard was created as another layer of safety for donors as well as patient groups who rely on plasma-based therapies. By maintaining a level of control over the donor population, a plasma center can help to ensure a steady and reliable donor population and supply of quality plasma (emphasis added).

The second relevant IQPP standard is the Viral Marker Standard. It is similarly concerned with risk reduction:

> Viral Marker Standard: It is important that donations are collected from a low-risk donor population. This standard focuses on that element. Each center is obliged to report its

> viral marker rates for HIV, HBV and HCV in the donor population. The center's rates are compared to the industry average. Alert limits are set to take into account the number of annual donations. If a center exceeds the limit for any of these viruses or the aggregate of the three viruses, the center will implement corrective actions that will bring the center into compliance with the standard.

These standards, referred to in the data, reflect two occasions where geographically specific subgroups of the entire donor population are mentioned, and thus discursively traceable.

Once again there are traces that reflect how these multiple discourses are related. According to Penrod (2011, 16), "The cornerstone of the image and credibility project, as well as the larger strategic objective of plasma, is the IQPP voluntary standards program," suggesting conversations regarding image, donor, and donor geography are discursively related. It seems likely that this particular geographic discourse, while a necessary component of risk prevention, is omitted from further discussion in *The Source* because industry leaders realize it is also connected to public scrutiny and the detriment of industry image.

It is also important to note that the term "profit" (or its derivatives) occur only 49 times in the data (< 0.0001 %), and it is completely absent from any link to clinic location. Consequently, while the IQPP standard covers clinic location and adjacent donor sheds, it omits the fact that the selection process for new clinics location most likely begins with a similarly spatial, but mainly monetary, assessment. These enterprises must be first, and foremost profitable. The selection process begins well before a single individual donor is evaluated as the IQPP standard are measured post hoc. Thus, communities are identified according to profitability before safety considerations.

Where there is discursive structuring of the donor, and the rarer associated geographic structuring, it seems to be carefully cultivated. It is possible that talking of communities and specific locations begins to paint a picture of the average donor that is concealed at scalar extremes. There are two instances in the dataset (not related to protocols) that include

descriptions of specific meso-scale donor geography. Both instances relate to cross border donating that occurs in the US/Mexico border (see chapter 1).

The first explicit reference to border clinics is reflected in a 2007 articled penned by Jan Bult, the PPTA president at the time. In his article titled "Source Plasma Collection in the USA" he discusses the IQPP standards and their role in ensuring that plasma is "collected from healthy donors who are free from diseases." One additional protocol that is mentioned is the marking of donors with luminescent ink to prevent over donation

> To ensure donor health, it is important that donors do not donate more than the allowed frequency. Common practice at many centers is to use a system where a donor's fingernail is first stained and then checked under an ultraviolet light prior to donation. The stain is not visible in normal daylight. Only when these checks are completed is a donor permitted to continue the process.

Given the persistence of discourses around donors as lifesaving altruists the most likely rationale behind this protocol is the risk of detriment to donor health motivated by an uncontrollable desire to do good in the world through donations. An alternative interpretation is that desperate donors are seeking additional funds in a country dealing with increasing economic precarity and shrinking social safety nets.

Bult (2007) addresses directly the question of clinic location, stating that, "Plasma collection centers are located throughout the country. They can be found in cities, rural areas and in some cases, along the borders." He also delivers a statement that was agreed upon by the PPTA Board of Directors concerning border clinics: "PPTA supports the collection of high quality and safe plasma from committed donors. Its IQPP standard program demonstrates that. PPTA does not provide guidance on the location of centers and accepts this as a company responsibility." It is noted that the statement was necessary after some discussion about centers located along the

United States border with Mexico, and their potential connection to exploitation and epidemiological risks.

Bult directly addresses the question of exploitation and the "concern about the social status of a Mexican national donating plasma in the U.S." Bult reasons that because Mexican nationals need a valid visa it is unlikely Mexican donors represent a population that is economically desperate. He cites the fee and strict requirements as barriers to exploitation. Most cases rely on a B1/B2 visa. This class of visa allows entry into the United States for a temporary stay related to tourism, shopping, visiting, or consulting. This visa type expressly prohibits working for pay while in the US. Despite Bult's assertion, it is certainly possible that people with these visas are in financial need.

Perhaps the most compelling evidence of donor geography construction follows immediately after Bult's (2007) piece, a biopic of a clinic manager in Eagle Pass, Texas, titled "Profile of a Hero." The author describes the geographic situation with exceedingly positive language, implying that impossibility of exploitative practices:

> Irma treats her donors like an extended family. As she makes her daily rounds to monitor operations, she is greeted by smiles and inquiries about her health, or the status of her soon to be born grandchild. She counters with her own questions about donor's children (many call her Tia or Aunt) and sometimes extends incentives for a good report card. When she needs a midday break, she takes a short walk in the fresh air to see the sun dappled palmettos and banana trees that accent the neighborhood. She knows by name the passersby on the sidewalk who call out hellos. This family atmosphere brings in the donors. There is a circle of life and hope that surrounds the day-today activities at Irma's center.

This passage seems to roughly align with Dixon and Hapke's concept of semantic geography. While the piece is not focused exclusively on an abstract space (i.e., the clinic at Eagle pass certainly exists), it is partially hypothetical as it is incomplete. It reflects one clinic, in one place, from one person's experience (the clinic manager) and is filtered through another's perspective

(the author). The piece certainly reflects a framing of physical space and thus can be considered a discursively produced geography - one that is imaginative and constructed to achieve certain ends. The intentionality of the author and the PPTA is impossible to determine. However, it is difficult to ignore the scalar void this geographic discourse seems to fill. The pleasant and family like atmosphere would likely help deter or rebut criticism of donor exploitation, a criticism that permeates through a meso scalar discussion of clinic locations and donor communities.

The topic of border clinics is broached again in a 2010 special issue that appears to be dedicated to donors, and includes pieces concerned with product safety, donor health, and donation ethics. The thrust of Bult's 2007 defense of border clinics is echoed. In the issue's reporting on the 2007 PPTA Stakeholder Report it is revealed that a principal item of discussion was "centers located along the U.S.-Mexican border and questions surrounding plasma donated by Mexican nationals in those centers." The topic was framed, in part, by

> the need to clarify the definition of U.S. plasma; safety of plasma-derived therapies; viral marker rates for border centers; the potential for donor exploitation; donor incentives; patient and public perception; and the opportunity for greater communication and awareness surrounding source plasma collection practices and plasma protein therapy fractionation.

According to reporting accounts, concerned stakeholders were reassured of the quality and safety plasma collected at border clinics, citing industry layers of risk assessment and management protocols. Many of the measures are reflected in the IQPP standards. To further demonstrate their safety the PPTA hosted a Westat, Inc. biostatistician to present information regarding viral marker rates and alert limits for HIV, Hepatitis B, and Hepatitis C with respect to clinics' review period, and factors that contribute to residual risk for plasma protein therapies.

Stakeholder concerns of exploitation were ostensibly alleviated by reference to US visa requirements

> Conditions for earning a visa into the U.S. were discussed, including the U.S. requirement for visa holders to be employed, and the costs associated with obtaining that visa, which provides limited access into the country. Further, the existence of a family atmosphere at the Texas border centers where donors expressed that they feel that they are helping others, while being fairly compensated, was reported.

A final article addresses the criticism of industry targeting of poor communities. Penrod begins by stating the process of donating is poorly understood and suggests remedying this with education. Education is a reoccurring mission/theme:

> The action point for many plasma centers, however, is within the local community. With national and international campaigns, and even endorsements by members of Congress and state governors, the neighborhood in which a plasma center dwells is the world that is experienced. Individuals, neighboring businesses and community groups who know only about rumors and jaded pictures provided by the industry's detractors are willing to fight against a plasma center. . . . Oftentimes, detractors will use "facts" and "figures" from decades ago, alleging that such derogatory portrayals of the past are valid today. Plasma collection centers. . . can always benefit from presenting the best and most positive aspects of plasma collection to the community in which they are located. It is time to replace fiction with fact!

A reoccurring mechanism is the magazine's avoidance of arguments centered on exploitation, similar to the scalar bias noted earlier. In Penrod's piece he presents the benefits a community can expect from hosting a plasma clinic including local employment and career opportunities, local circulation of capital through donor compensation, and growth of the tax base. The reluctance to engage with the question of exploitation in an elemental way may stem from the organization's recognition that a thorough treatment of the topic would be unpalatable for many in the public eye. It would likely require a more detailed description of donor communities, the logic of industry locating practices, definitions of labor and donation, and the lucrativeness of the industry for stockholders and investors relative to the average donor (the ostensible cornerstone of the entire industry).

Conclusions

There is a set of historical debates over plasma collection practices, with some centering on epidemiological risk, economic philosophy, and ethics. In the midst of these long and ongoing debates the example of *The Source* demonstrates their linkages. The major discourses identified provide some evidence of the connections.

Not all of the articles concern precisely and explicitly industry image and donors, but given the industry's history, these discourses make sense, and they suggest industry efforts to structure conversations in a way that benefits private fractionators, sometimes to the detriment of public institutions. The structuring of a positive image discourse was so explicit and obvious, it may not even qualify as a discourse or linguistic trace. However, identifying and exploring the efforts to structure a positive image were necessary to identify the others (donor and donor geography). Perhaps most interesting was the identification of a geographic discourse that was structured first through selective scalar framing in conversations surrounding donors. Save for two exceptions, the geographic discourse was also structured by the omission of meso-level references to donors and donor geography surrounding clinics. The two exemptions focused on clinics at the US/Mexico border. Notably the articles were responses to concerns voiced by stakeholders, suggesting that, without prompting, the references and discussion of ethics and safety would have been avoided. Further, neither adequately addressed the concerns of exploitation. That the scalar framing may be intentional was supported by industry's IQPP epidemiological protocols acknowledging the importance of subsects of the donor populations and the donor sheds surrounding clinic locations.

CHAPTER III

A GEOGRAPHIC PERSPECTIVE OF THE BLOOD PLASMA INDUSTRY AND ITS ORIGINS

Abstract

The blood plasma industry is unique and as such provides challenges to widely adopted understandings of economic geography and globalization. This paper begins by providing a brief history of the blood plasma industry. Next, the paper highlights the conceptual challenges posed by plasma in two ways. First, by comparing the economics of plasma to labor and natural resources, it is demonstrated that plasma does not fit neatly into either economic category. The second conceptual challenge is related to the important role the US plays in the modern global market as the leading supplier of raw plasma. It is suggested that given the skill prerequisites of plasma donation the US's status as the OPEC of plasma makes little sense from the perspective of mainstream geo-economic theory. The paper concludes by offering some explanations of the US role in the plasma market.

Key words: plasma, plasmapheresis, economic geography, Global Shift

Introduction

Despite having the trappings of both commodified labor and natural resources, this paper demonstrates difficulties that accompany conceptualizations of the global plasma market. This paper focuses on the developmental history of the global plasma market as it related to orthodox economic geographic theory and its treatment of labor and natural resources.

Conceptualizing plasma at the local scale has also been problematic (see chapter 1). It has been described as a natural resource important to national security (Strengers and Klein 2016).

It has also been described as a gift and commodity (Hagen 1982). In the case of the US it is unclear if plasma and plasma donors should be thought of as pools of labor or a natural resource. Moreover, it is unclear if clinics adhere to the logic that often guide locational descensions of actors and firms in the service sector. The additional layer of bordering practices from nation-states may also reveal structures of the plasma economy at the international level not observable within the US (see chapter 1).

The remainder of this paper continues as follows. First, a historical survey the blood plasma industry, noting keyed developmental milestones, including innovations in production, medical application, market restructuring, and public health crisis is provided. Second, the evolution of the industry is scrutinized from a geographic prospective, specifically how the industry's evolution is unusual when compared to other sectors, industries, and actors in economic geographic literature. Finally, the paper reflects upon the complexities arising from the nature of blood plasma and the limitations it places upon modern theories of economic geography.

History

The historical survey draws upon three important texts (Hagen 1982; Starr 1998; Farrell 2012). Hagen's (1982) *Blood: Gift or Merchandise?* provides a detailed account of newly organized transfusion services in industrialized countries. The author highlights the global problems resulting from the worldwide dependence on paid blood donors, and in particular, from the development of private collection clinics. Without condemning the principle of paid donors and the development of blood products by private enterprise (for a contrast in approach see Titmuss 1971), Hagen highlights ethical challenges encountered by medical professionals early in

the development of for-profit clinics and manufacturers of blood products. Hagen's research stopped in 1981, just short of the AIDS epidemic.

Starr's (1998) *Blood: An Epic History of Medicine and Commerce* is a journalistic account of blood and plasma's transformation beyond scientific curiosity by commercial forces. Starr covers important transfusions milestones in from the seventeenth through the early twentieth centuries. More importantly he focuses the development of an international blood-products market and the effect of AIDS on the blood industry. Despite its journalistic approach his book is widely considered to be well researched, containing many references to primary source documents and interview material. As such, it fills a void in scholarly literature on the topic and is regularly referenced in academic and non-academic contemporary work (Farrell 2012; Garner 2018).

Anne-Maree Farrell's (2012) *The Politics of Blood: Ethics, Innovation and the Regulation of Risk* examines the inter-relationship between politics, ethics, and law in governing risk of blood. She focuses her research on England, France, the United States, and the European Union. Farrell's work includes substantial historical research because of the complex questions she addresses. She considers different conceptualizations of blood (blood as a gift, blood as commodity) and donors, and the potential benefits of each. This requires a historical review of these conceptualizations and how they may have changed. While Hagen notes important commercial "moments," Farrell identifies important political shifts (i.e., the politization of blood in the 1980s). Farrell's work, like Hagen's is scholarly and measured.

There is a distinction between blood and plasma. This is reflected in the historical evolution of transfusion medicine. The normative claims related to this distinction is also the subject of modern debates over the ethics and regulatory policy concerned with national blood

systems. Blood is a specialized body fluid that fulfils a variety functions including transport of oxygen and nutrients to the lungs and tissues, clot formation to prevent excess blood loss, transport of cells and antibodies to fight infection, transport of waste products within the blood to the kidneys and liver for filtering, and regulating body temperature. Blood has four constituent parts, or components: plasma, red blood cells, white blood cells, and platelets. Plasma is the straw-colored liquid portion of blood that suspends the other components, aiding mainly in transport. Plasma is constituted by a mixture of water, sugar, fat, protein, and salts.

Medical understanding of blood preceded plasma. Scientific efforts toward understanding blood date to the 17th century. Certainly, the importance of blood extends even farther back, as it has long been imbued with socio-cultural meanings (Camporesi 1996; Farrell 2012). It has been suggested that plasma was discovered as early as the 16th century (Wintrobe 1980). However, its importance was recognized by Karl Landsteiner in 1900. Landsteiner discovered the presence of isoagglutinins in human blood which reacted with the red cells of a certain types. This discovery led to identification of the A, B, AB and O blood types. Further research revealed blood was composed of plasma and several cellular components (red cells, white cells, and platelets). Still, Schmidt (2012) describes plasma as " the first blood component" and locates its "birth" in the early 1940s, likely because additional major breakthroughs toward understanding plasma were achieved much later, well after whole blood transfusion medicine was common place (see also Highlights of Transfusion Medicine History 2019).

The global plasma market has grown substantially in the past thirty years and owes its current lucrativeness to two historical scientific breakthroughs: fractionation and plasmapheresis. As a response to the need of blood toward war efforts the US government enlisted the help of Dr. Edwin Cohn, a Harvard University protein chemist. At the time, transfusion of whole blood or liquid plasma were the only two options for treating wounded

soldiers. In 1941 Cohn developed the process of fractionation, a technique that allowed separation of plasma into protein-based component parts, or fractions (Hagen 1982). A result of this process was the development an important fraction called albumin, which proved to be a logistical improvement over both liquid plasma and whole blood in the treatment of wounded soldiers. The technique that came to be known as Cohn fractionation, was integral to blood component therapy in the latter half of the twentieth century (Starr 1998; Farrell 2012). By 1942 the US government invited private commercial firms to develop fractionation on an industrial level. The first manufacturing plant for plasma products was established in the 1940s. The plant was located in the USA and operated by a company known as Cutter (Hagen 1982).

Plasmapheresis was another advancement that aided the growth of plasma collection and manufacturing from a primarily local endeavor into a global activity (Burnouf 2007). Since plasmapheresis allows for plasma extraction from donor whole blood and the retention of red and white blood cells, donors may donate plasma more frequently. Plasmapheresis was pioneered in the 1950s by the Spanish company Girfols (Hagen 1982). According to Farrell (2012, 38), plasmapheresis "enabled the burgeoning industry to collect plasma from individuals on a weekly basis which could result in up to fifty liters of plasma being taken from a single donor on an annual basis." The combined impact of Cohn fractionation method and plasmapheresis led to the expansion of the industry by the end of the 1960s (Farrell 2012). In 1965 Judith Pool discovered that freezing and slowly thawing plasma produced factor VIII. This residue, which became known as cryoprecipitate was a substantial improvement over plasma's ability to promote clotting in hemophiliacs. Factor VIII was again improved upon to produce a purified clotting factor VIII powder, known as factor VIII concentrate. With each improvement in clotting properties the factor concentrates require additional plasma to produce a single unit. Producing a small amount of concentrated factor VIII required thousands of plasma donations. It became apparent that an

economy of scale could be achieved by increasing the size of vats used in fractionation. The motivation to produce cheaper products through economies of scale would eventually contribute to large scale contamination.

The plasma protein market has steadily grown in terms of value and throughput since the late 1990s. The industry's global value grew from $4.8 billion in 1996 to $11.8 billion in 2008, reaching over $21 billion in 2016 (Wellington 2014; Hotchko and Robert 2018). The volume of plasma fractionated annually by the pharmaceutical industry has grown from 28 million liters in 1999 to 45 million liters presently, with the majority provided by paid US donors (Volkow and Del Rio 2005; Burnouf 2018; Weinstein 2018).

Geographic Perspective

Blood plasma's economic geographic dynamics are unique. Previous work has explored the ethical considerations of conceptualizing plasma (gift vs commodity). Previous geographic research has also demonstrated that conceptualizing plasma to empirically model it at a local scale or situate it into a policy category is also difficult. These previous observations focused on plasma clinics within the US. It was noted in chapter 1, for the purpose of highlighting the unusual nature of paid plasma exchange, that the demand for US plasma is driven by global export demand. But there was no analysis of how the US became the global leader in plasma exports.

Openshaw (1981) demonstrated that spatial phenomena are capable of presented different and even conflicting patterns when viewed at different scales. Similarly, an analysis of US clinics, despite the US's importance to the global industry, cannot provide a complete picture of the geographic and historic dynamics of the global plasma market. A broader geographic perspective can further determine plasma's 'unique' dynamics.

Clinic locating practices are guided by a plethora of inputs and can be influenced by multiple scales and layers of institutional, cultural, and political practices. Theoretical frameworks for specific and local choices are difficult to describe because these phenomena are more idiographic in nature. However, the global distribution of economic phenomena aggregated at the nation state-level (i.e., location and collection practices globally) may be more generalizable theoretically.

This paper compares different conceptualizations of plasma to other major economic inputs. Specifically compared are the geographic nature of plasma and other well theorized economic inputs and activities. The plasma industry, along with global clinic locating practices, are compared to other sectors and inputs as conceptualized in Dicken's (2015) influential work *Global Shift*.

Dicken's work serves as a foil for two reasons. First, it is one of the most significant contributions to the field of economic geography, especially in the realm of orthodox economic understandings of globalization. First published in 1986, and now in its seventh edition, *Global Shift* aims to explain international economic change through the global behavior and strategy of transnational corporations (TNCs). Second, Dicken argues for a cross scale perspective to approach economic globalization, suggesting that understanding industrial restructuring at the regional scale requires assessments of phenomena taking place at the world scale, particularly as it pertains to organizational strategies of TNCs. Similarly, this paper rests upon the notion that understanding the locating practices of plasma clinics in the US can only be understood by an evaluation of global/international economic developments. Finally, Dicken's work is truly expansive in that it includes numerous case studies of major sectors and inputs. Other classic works focusing on globalization, like Massey's (1995) critical Marxist approach concentrates on manufacturing (Massey 1995; Phelps 2008). The first edition of *Global Shift* focused on the

manufacturing shift, though later editions expanded in order to include the service sector and cases studies in natural resource extraction.

To scrutinize the evolution of the industry from a geographic prospective, tracing the industry's history, along with significant events that shifted its geographic footprint, this paper demonstrates that the blood industry's evolution is unusual when compared to other industries. Special attention is given to the place of the United States in the modern global market, which is argued to provide insight into broader economic mechanisms.

Natural Resource or Labor Pool?

Natural resources (i.e., starting materials) are the most geographically embedded of economic inputs. This geography is often only disrupted through technological advancements. Dicken (2015, 396) states that "The basis of the extractive industries is the notion that of the natural resource: materials created and stored in nature through complex biophysical processes over vast periods of time." He also notes that the natural resources are socially constructed (e.g., crude oil was of little worth until the turn of the 20th century). The finite nature of most natural resources, their fixed locations, and territorial embeddedness together create a particular economic geography. Like other natural resources, a single unit of raw plasma may be collected in one place, refined or manufactured in another, before finally being consumed in yet another (see Figures 16 and 17).

The industry's clinic locations reflect some of the globalizing processes and patterns described by Dicken. For instance, Dicken suggests that much economic development can be understood through the lens of TNCs. TNCs have emerged in the past forty years as splintered networks, exhibiting 'footloose' behavior explainable as strategic choices aimed to maximize profit. CSL provides an example. CSL Plasma operates one of the world's largest and most sophisticated plasma collection networks (more than 230 plasma collection centers in U.S.,

Europe and China). CSL Plasma is vertically integrated, meaning plasma collected at CSL Plasma facilities are used by CSL Behring for the sole purpose of manufacturing and delivering pharmaceuticals. CSL Behring is a global biotherapeutics company but is also only one of many companies belonging to the parent company CSL Limited. Each of the corporate networks operates out of different places. CSL Behring is headquartered in King of Prussia, Pennsylvania; CSL Plasma is headquartered in Boca Raton, FL; and CSL Limited is located in Melbourne, Australia.

There is another similarity between plasma and extractive industries that have undergone globalization. Plasma evokes strategic considerations. Strengers and Klein (2016) describe it in terms typically seen in discussion of energy security.

> The majority of plasma supplies for the manufacture of PDMPs is met by the US commercial plasma industry. However, geographic imbalance in the collection of plasma raises concerns that local disruptions of plasma supplies could result in regional and global shortages. . .. Plasma, which fits the definition of a strategic resource, that is, "an economically important raw material which is subject to a higher risk of supply interruption," should be considered a strategic resource comparable to energy and drinking water.

They suggest ensuring a reliable supply of plasma will require national and regional policies changes. They also advocate an equitable balance of the international plasma supply to reduce the risk of shortages and ensure plasma impendence.

However, there are noted departures in the geographic pattern of plasma extraction compared to other natural resource activities. The most apparent difference is their location specification. Discussing natural resources Dickens describes their spatial embedded-ness as “they are where they are.” Stated differently, plasma is not literally fixed in the environment. Plasma exists in all humans across the globe, though not all plasma is of the quality desired by fractionators.

This may partially explain why there is no persistent resource curse affect associated with countries that export plasma. The resource curse describes the political and economic impacts experienced by countries endowed with large mineral resources or energy reserves (Sachs and Warner 2001; Watts 2004; Billon 2008; Ross 2015). Interestingly, the phenomenon is not totally absent from the history of plasma.

The resource curse has historically been associated with more durable authoritarian regimes, increases in certain types of corruption, and violent conflict in low- and middle-income countries (Ross 2015), though this link has been debated (Haber and Menaldo 2011). The ills of the resource curse are usually sustained because of export demand from more developed countries, along with more developed countries enabling or supporting the regimes supplying cheap raw materials.

During the 1970s, the international trade in plasma grew. According to Hagen (1982) all of the headquarter countries of the major firms were in wealthy westernized countries, and much of the plasma products were exchange between the same countries (see also Starr 1998). Additionally, plasma market exchanges were concentrated in cities like Montreal and Zurich (Farrell 2012). During this period there were instances in which national plasma supplies resembled the type of resources that have been associated with the resource curse. Companies involved in the industry established or encouraged third parties to establish clinics in less developed countries.

During this period US backed Nicaraguan President Anastasio Somoza was a part owner in a company named Plasmaferesis. The company was established in the 1970's by Pedro Ramos, a right-wing Cuban doctor that fled during the Cuban Revolution in 1959. The company was made profitable by extracting plasma from poor and desperate Nicaraguans and then selling it to Europe and the United States at a substantial mark up. A company named Hemo Carribean

opened in Haiti and engaged in similar activities. Hemo Carribean was owned by Joseph B. Gorinstein, an American stockbroker. Hemo Carribean had negotiated a 10-year contract with the Haitian Government President Francois Duvalier and operated under the tenure of Jean-Claude Duvalier. Both presidents developed reputations associated with despotism and corruption. Other developing countries where this pattern repeated included Lesotho, Belize, Dominican Republic, Costa Rica, El Salvador, and Colombia (Starr 1998; Farrell 2012). These clinics eventually closed because of condemnation by the Red Cross and the World Health Organization (Farrell 2012). During this brief period of exploitation, the trajectory of plasma collection simultaneously resembled manufacturing labor shifts.

The global economy of plasma is also potentially analogous to labor. The most striking similarity is that the process of plasma collection involves humans. Donors offer their time and plasma in exchange for compensation. Within the US, at the local level, the spatial distribution of clinics somewhat reflects the firm location patterns one might expect from companies seeking a appropriate labor pool. Collectors are searching for donors that are willing to sustain a supply of plasma for as little compensation as possible. This is similar to the pattern describe by Dicken's account of the global shift in manufacturing:

> Over a period of 300 years or so, a global division of labor developed and intensified with industrialization, in which newly industrialized economies of the West. . . became increasingly dominant in a core-periphery configuration. . .. The broad contours of this core-periphery global economic map largely persisted until the outbreak of the second world war in 1939.

Decreases in transportation and communication costs allowed manufacturing firms to locate in countries that had weaker government regulations and little to no history of organized labor.

Escaping the major infrastructural damage caused by two world wars, the US emerged as a major core of manufacturing activities. Much of Europe, along with Australia and Japan would eventually become core actors in manufacturing as well. The processes of globalization and deindustrialization during the 1970s would later impact these countries, reducing their share of manufacturing as a proportion of total employment. Whereas manufacturing fled the US and Western Europe for cheaper labor in less developed countries, plasma collection concentrated in these places (Figure 16). Compensated plasma donation would seem destined as part of the developing world's economy. Donating requires virtually no skill. Starr (1998) has reported that literacy is not universally enjoyed by American donors. How then could it be that developing, and newly developed countries have not emerged as a primary source of plasma, rather than the US, one of the wealthiest countries on the planet? Further complicating the understanding the distribution of collection, is the distribution of consumption by nation. Plasma derived products are nearly exclusively consumed by the world's wealthiest countries (Figure 2).

Figure 16. US Plasma Transfers

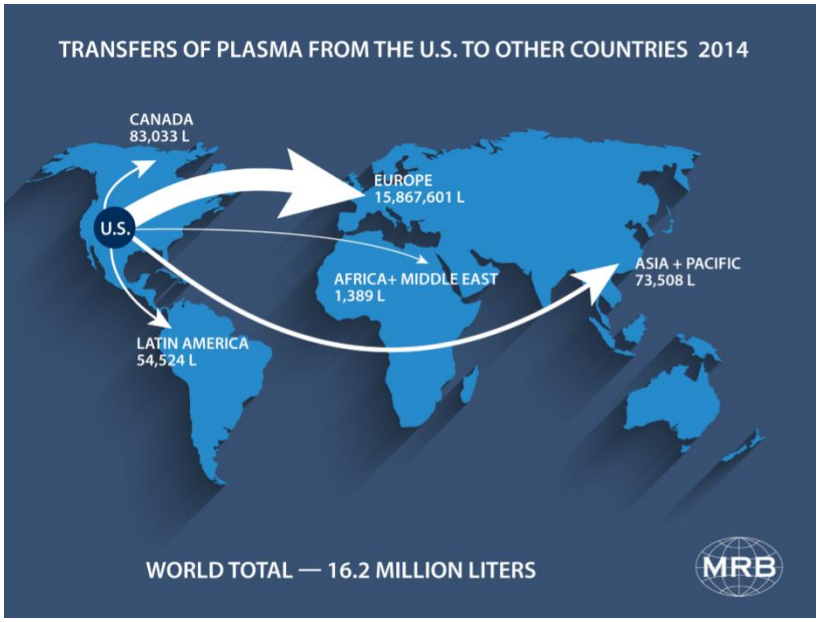
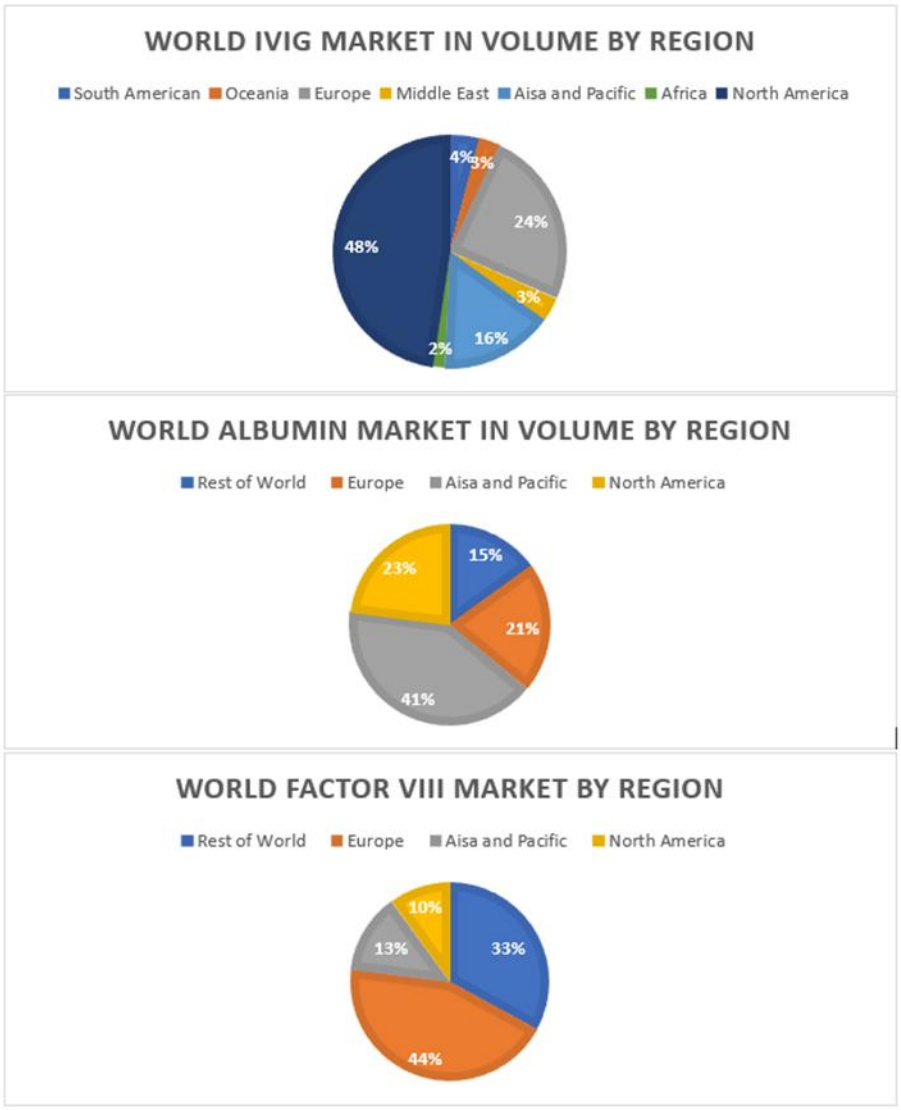


Figure 17. Plasma Market Summary



The Role of the US

The supply in plasma-derived medicines relies on the availability of plasma collected from human donors. The total volume of plasma fractionated worldwide in 2010 by 78 fractionators was slightly over 33 million liters. Most plasma collection/fractionation capacity is in North America and Western Europe. The supply of plasma for fractionation was historically

based on voluntary whole blood donations and plasmapheresis from volunteer donors. In addition, in the United States and certain European countries, plasmapheresis is collected from remunerated donors. Remunerated plasma generates the additional volume required to meet growing product demand. Today, 75% of the plasma used for fractionation is obtained by plasmapheresis (Burnouf 2011).

The world supply of plasma derivatives is dependent on US source plasma, which uses compensated donors and is exempt from FDA requirements that govern whole blood collection. In 2010, it was estimated that 51% of the world's supply of plasma for fractionation was generated by the US source plasma sector (Farrugia, Penrod, and Bult 2010). Wellington (2014) reported that US donors constituted 70% of worldwide collections. More recently, Hotchko and Robert (2018) estimated that 66% and 74% of total and sourced, respectively, came from the US. The US is unique in that it has adopted an almost entirely laissez faire framework to plasma procurement. Other countries have taken decided stances on the market-based approaches to blood by either prohibiting monetary compensation or strictly limiting the number of donations allowed.

The category including plasma (i.e., Plasma, vaccines, blood) was ranked 11th in 2019 among the roughly 1,265 US export commodity groupings as classified by Census. It ranked No. 12 for the last full year with a total value of $23.21 billion, a 14% increase from the 2017 total (US TradeNumbers 2020).

Despite impressive growth, there remain limitations on economically conceptualizing plasma. Further this adds difficulty in understanding the US's role in the evolution of the plasma economy. Despite Dicken's inability to deal with plasma economics, his larger understanding of global supply chains is helpful. He describes one layer of the tangled web of economic connections as "geographically-specific configurations of socio-cultural practices and

institutions." Indeed, it seems that historical contingencies and cultural differences help partially explain the US's role as the leading supplier of plasma to the world. The remainder of this section explores some of the reasons for the US's importance to the global plasma economy. First discussed are peculiarities of the US, specifically its historical contingencies and cultural traditions. Second, some examples from other countries are provided for the purpose of contrast. An exhaustive comparison is beyond the scope of this paper. The examples provided simply offer partial support of the general thesis that the US's history and political cultural account for its current success in the global market.

There are two separate but related potential explanations for US dominance as a supplier of plasma. First, are the historical contingencies surrounding the birth of plasma collection and manufacturing. After WWII major differences emerged in how national blood systems were governed. The most noted distinction being the willingness of state government to allow private interests to establish a presence.

Many developed countries established programs for the collection of peace time blood supplies. While some countries relied on the Red Cross, others opted to create state agencies to manage national blood systems. Despite cooperation during the war period, major conflicts between US non-profit blood organizations emerged (Hagen 1982; Farrell 2012). Governments in other developed countries provided financial and institutional support for the development of not-for-profit and state organized collection and manufacturing. Two key organizations that sought control of whole blood collection and supply in the USA were the American Red Cross and the American Association of Blood Banks. According to Farrell, ongoing tensions between the two organizations accounted for the lack of a unified and national approach to whole blood collection after WWII.

After WWII the American Red Cross was committed to forming a national presence in blood collection and supply, but because there were already existing locally organized banks it only expanded into area that invited. The Red Cross also took the view that non-medical personnel could be involved in the management of collection operation, though requiring physician support. The Red Cross supported centralized over localized control, in regard to management of blood collection. Finally, as it does today, the organization promoted only the voluntary donation of whole blood, emphasizing community responsibility, and no requirements upon recipients. At the time the aim was to create support for blood donation through appeals to patriotism since it had been effective in the war period (Farrell 2012).

Independent or community blood banks run by physicians coexisted during the Red Crosses expansion efforts. These banks and their interests were represented by the AABB, a national body that had been formed in 1947 (Farrell 2012). Red Cross efforts to establish a national presence were met with consternation, possibly because the Red Cross represented economic and ideological opposition. Ostensibly the AABB viewed the role of non-medical personnel involvement in management as usurping the established role of physicians. Starr (1998) suggests that the AABB was actually established with the sole purpose of challenging the Red Cross, an organization consider socialistic.

In contrast to the Red Cross, the AABB emphasized local autonomy and professional control of blood collection. They advocated for a more individualistic philosophy of exchange. Individual responsibility governed operations whereby individuals receiving blood were expected to contribute towards the replacement and/or cost. The AABB established a national clearinghouse where hospitals and local blood banks traded blood and blood credits, with repayment being in the form of money or blood (Farrell 2012). Arguably it was the inability to reach consensus from the leading non-profit organizations that allowed commercial and for-

profit interests to take hold in the US. The pattern here resembles the contradictions and failure prone to the liberal tradition (Deneen 2019; see also chapter 2). Commitment to individualism potentially leads to over-commodification. Eventually this logic encroaches upon what were considered public goods and acts of civic commitment. As a result, civic and group solidarities are eroded. One might expect to be left with a market governed group of reasonable individuals. However, as critics of neoliberalism have shown the actually outcome is the rise of solidarity among commercial interests and society's economic elite (Harvey 2007).

As Farrell (2012) suggests, path dependency (economic and institutional) is a partial explanation for the dominance of the US. Since the US first developed the fractionation method, private US firms involved in fractionating plasma were well positioned. The timing was certainly fortuitous for the US. Many countries' industrial capabilities were shattered by WWII, but the plasma industry was born during the period. Additionally, the integration of fractionation and collection also help explain the US dominance of the industry. In the late 1970s fractionators began acquiring regional and independent collection clinics, and large-scale mergers and buyout have continued.

By the 1980s, the gift relationship had become inextricably linked to self-sufficiency policy and was seen as an important objective to be realized on ethical, economic, and safety grounds. In the cases studies of France and England, Farrell (2012) found that, despite being nationally organized, state blood systems lacked centralized and standardized protocols which contributed to inefficiencies. By the start of the 1980s, collection operated as a niche within the global pharmaceutical industry. There were six companies at the time that controlled most of the world's plasma. Most of these companies were based in the US (Farrell 2012).

The second potential explanation for US dominance relates to economic culture. Hagen (1982) argues that the determination of how blood supplies were organized were determined by

the “peculiarities of national, historical, and social developments,” rather than economic considerations. However, this would ignore the respective political cultures of these countries, and what ‘economic’ meant in some national contexts. As seen in previous discussions, there can be fundamental disagreements over the boundaries of economic logic. This seems to be reflected in disagreements over conceptualizations of plasma and how it should be collected and managed.

In countries that viewed blood as part of the common good, blood and plasma products were not differentiated. This gift relationship understanding of blood (and especially plasma) was resisted in the American context. The blood vs plasma distinction, and subsequent two-track system that emerged in the US, allowed more flexible regulatory standards. This flexibility was vital to US success as it allowed US companies to be well poised for the coming boon in plasma. The two-track system emerged out of the FDA compromise concerning donor payments. On the one hand there were serious economic interests from US plasma fractionators to be able to procure paid plasma, arguing that demand simply required it. On the other hand, advocates for an all voluntary system pursued completely banning payments for blood components. Rather than banning compensation the FDA decided to compromise with a labelling requirement indicating the material origins. The consequence of this was that whole blood became an all voluntary endeavor while plasma continued as a paid enterprise.

The US cultural norms that created the conditions for the possibility of a for-profit sector influential enough to broker the compromise is a separate question. These norms are likely deep seeded. In his reassessment of Alexis de Tocqueville’s Democracy in America, Swedberg (2009) argues de Tocqueville’s had a highly original and suggestive approach to economics — one that still has much to offer. Tocqueville saw US society as moving from aristocracy (or a small elite controlling all resources, including economic ones) to democracy (or all resources being increasingly shared, including economic ones). Tocqueville noted that the United States had been

shaped by four causes. Besides the shift toward equality, there were also the English influences, puritanism, and commerce. Swedberg suggests a closer look at US economic culture provides a better sense of economic dynamics during the time of Tocqueville's visit:

> Buying and selling seemed to be happening everywhere, not only according to contemporary observers but also according to modern historians. There was "a frenzied race for riches," and a "speculative spirit was everywhere," to cite a standard work on the Jacksonian period. It was also around the time of Tocqueville's visit that such expressions as "self-made man," "businessman," and "millionaire" made their historical appearance in American language.

Swedberg also notes that

> Prominent in Tocqueville's mind . . .were the entrepreneurial spirit in the United States, the new class structure that was emerging, and the centrality of economic matters to U.S. culture more generally. One of Tocqueville's most enduring impressions of the U.S. economy was . . . that it was deeply entrepreneurial in nature. There was an unmistakable "spirit of enterprise" in the country, as he put it. Americans were very inventive and innovative in economic matters. "Almost all of them," according to one of his notes, "are real industrial entrepreneurs." *The entrepreneurial attitude that was so strong in the economy also extended to other areas of society*. Tocqueville was, for example, fascinated by U.S. religious leaders, who at one point in his notes he calls "entrepreneurs of religious industry." (my emphasis)

The emphasized section of the passage is one early example of non-market activities being captured by economic logic and arguably eroding group solidarity.

Given the possibility that the US's successfulness and willingness to permit compensated plasma stems from longstanding and deep seeded political and cultural foundations, one may also draw upon historical and cultural factors of other countries to explain the unwillingness. This potentially provides some insight into why the organization of blood systems emerged as they did, and why the US differed so markedly. Specifically, it may be the entrepreneurial spirit of the early US that was so influential. European countries tended to adopt the gift-based conceptualization of blood and either nationalized the industry all together or significantly

restricted private enterprise. One might describe some of the resistance to the American model in some European countries as cultural barriers. These cultural concerns manifested differently in other parts of the world. For instance, barriers to plasma trade in India exist on religious-cultural grounds (Copeman 2008).

To understand European hesitations in pursuing a system of plasma collection similar to the US, one might consider the corporatist legacy of Europe, along with its status as the hearth of nationalism and the nation-state ideal. Corporatism is a political system in which authority is given to specific unelected groups (i.e., corporations) to make decisions within a state. The groups represent economical, industrial, and professional interests. An early and important theorist of corporatism was Adam Müller, an advisor to Prince Metternich (in what is now eastern Germany and Austria). Müller articulated corporatist views as an antidote to two dangerous trajectories: the egalitarianism of Revolutionary France, and the laissez faire economics of Adam Smith. This suggests why corporatism has been viewed as an economic third way (Sitnikov 2013).

Despite varying opinions on its connotations, fundamentally, corporatism supports the idea that the community and economy of a state have to be systematized into main interest groups, with representatives of those groups resolve conflict through debate (Sitnikov 2013). According to Sitnikov (2013) in Germany and elsewhere there was a distinct aversion among to allow markets to function without state guidance. This reflects general culture heritage of Europe that stem from the medieval era, one adverse to individual self-interest. Market mechanisms were closely governed by a collectivist sentiment and social regulation.

In the case of both England and France, VNRBD had become inextricably linked to the war effort, representing an affirmation of all that was good about bonds and obligations of

citizenship, whilst at the same time having its historical roots in nineteenth-century thinking about the relationship between blood, race and nationhood.

The manifold applications, approaches, and tensions of European corporatism are evident in the history of blood management in France. Following WWI, most, but not all, nations that clearly adopted a corporative framework were fascist governments. Additionally, in these fascist regimes, corporatist forms were mainly a façade for dictatorship and state repression of free trade unionism. In France. like the US, both paid donation and VNRBD continued to be used during and immediately after WWII. However, personnel involved in paid donation became associated with the Vichy regime, which cooperated as a puppet government for the Nazis during the war. Conversely, those involved in VNRBD were associated with the French Resistance (Farrell 2012). Farrell also notes that VNRBD eventually become the norm but was both hard fought and became linked to broader political disagreements. This accounts in part for France's lasting commitment to VNRBD. The lack of different group solidarities may be one of the conditions that made the US's eventual dominance possible. It may also help explain why the Red Cross was demonized as socialistic, and the weakness of American non-profits to retain control over the plasma system.

However, plasma self-sufficiency is often related to a sense of another solidarity, nationalism. In addition to being the hearth of corporatist political structures, it also marked the starting point of the nation-state ideal. Indeed, the self-sufficiency goals, and trade barriers, of Japan are likely connected to the nation-state ideal and a strict sense of national identity - traditions that were imported from Europe. According to Robertson (2012) during Japan's late 19th century modernization efforts blood became a vital part to 'performing' Japanese identity and was influenced by European ideas of eugenics. Yūsei Undō (Eugenic Exercise/Movement Association) was founded in 1926. The organization's leadership were committed to both

maintaining and improving the quality Japanese blood (Robertson 2002). In this context blood was viewed as

> the agent that determines outward appearances (e.g., phenotype) and performances (e.g., kinship relations), and that materializes that which is unacknowledged (e.g., membership in an indissoluble hemato-national community) . . . (Robertson 2014)

Prior to the mid-1960s, most blood donations in Japan were purchased from impoverished donors. However, in 1964 US ambassador to Japan, Edwin Reischauer contracted hepatitis from a blood transfusion during emergency surgery. Following the incident Japanese government quickly adopted a resolution to promote the voluntary donation of blood from screened donors. Since the scandal in the mid-1980s involving the use of unheated imported blood products infected with HIV, the Ministry of Health, Labor, and Welfare, have made self-sufficiency in the supply of blood a priority. The practice of procurement highlights the cultural and nationalistic undertones

> Implicit - and sometimes explicit, depending on the source - in the rhetoric of self-sufficiency is the assumption that Japanese blood is a unique and vital cultural resource that will ensure the future health of the otherwise resource-poor island nation (Robertson 2014).

There are likely objections to the notion that the US lacks solidarity (or its cultural requisites), as the US is often considered extremely nationalistic, even if not by its own citizens (Pei 2003). However, the US's nationalism differs from European countries and Japan. Zelinsky (1988) notes that the US is strikingly different from most 18th and 19th century nations. Perhaps most importantly to understanding the US's uniqueness, and subsequent lack of meaningful national solidarity, is that liberalism served as the ideological basis of the US's national identify. The application of liberal ideals in the early US nation and state were not encumbered with pre-

existing forms of communal bonds, as had been the case in other 18th and 19th century nations (Zelinsky 1988). Thus, the bonds of nationalism, traditionally understood, could not create the foundation required to support anything other than a liberalized and individualistic system of blood and plasma.

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